Schizophrenia is a major psychiatric condition, which affects the centre of the personality, with severe problems of perception, and cognition as well as affective and social behaviour (Do, Trabesinger, Kirsten-Kruger et al., 2000). There are currently no diagnostically relevant biological markers for schizophrenia: thus, schizophrenia is diagnosed according to internationally accepted clinical criteria, such as DSM -IV (APA, 1994). The concept of positive and negative symptoms (derived from the work of Jackson [1931]) was re -introduced in schizophrenia by Strauss and his colleagues in 1974 (Provencher, Fournier & Dupuis, 1997). Positive (Type I) symptoms are defined as a distortion or exaggeration of normal function. These include: thought disorders (disorga nised, irrational thinking), hallucinations (perceptions of stimuli that are not actually present), and delusions. In contrast, the negative (Type II) symptoms of schizophrenia (based on the concept of deficit) are defined as a diminution or loss of function and represent the absence of behaviour or function that is usually present in the normal individual: flattened emotional response, poverty of speech, lack of initiative and persistence, inability to experience pleasure and social withdrawal (Crow, 1980) .

Biological explanations of schizophrenia have received, by far, the most support (Comer, 2001). Nonetheless, several biological theories (e.g. genetic theory) are of limited value in accounting for the specific symptom types of schizophrenia (i.e. positive or negative): often merely emphasising the predisposition to inherit schizophrenia. Furthermore, in recent years, with technological advances, biological theories of schizophrenia have focused on chemical processes and structural and functional brain abnormalities (Carpenter & Buchanan, 1994), which are of greater value in terms of an explanation for specific symptom types. Therefore, the following literature will focus predominately on such biological theories, and discuss their value in accounting for both the positive and negative symptoms of schizophrenia. It will conclude that, on the whole, biochemical and functional and structural brain abnormalities do provide an adequate account of both the positive and negative symptoms of schizophrenia, when viewed as interconnected factors, which lead to disturbances of thought, perception, cognition, and social behaviour.

Dopamine, one of the major catecholamine neurotransmitters in the human brain, regulates a number of physiological functions, including mental activities, emotions, and hormone secretion (Himel, Koh, Sakai, Inada, Akabame & Yoneda, 2002). Research has demonstrated the presence of several dopamine receptor sub types (D1, D2, D3, D4, D5) in the brain; and four major dopamine pathways, three o f which are implicated in schizophrenia; the nigro -striatal, the Mesolimbic, and the Mesocortical (Wickens, 2000). The Nigro -striatal pathway, which projects from the substantia nigra to the basal ganglia, plays a role in the brains motor system. Tardive Dyskinesia, a side effect of several conventional antipsychotic drugs, is thought to occur due to dopamine being blocked in this pathway (Van Os, Walsh, Van Horn et al., 2000). The mesolimbic pathway, which links to the limbic system, is thought to play a c ausal role in schizophrenia. The limbic system is a major component in emotional regulation, and contains the nucleus accumbens - part of the brains reward system (Wickens, 2000). Psychoactive drugs, which produce rewarding effects, increase dopamine in this structure. Finally, the third pathway implicated in schizophrenia is the mesocortical pathway that projects from the ventral tegmental area (VTA) to the frontal cortex and surrounding areas (Rosenzweig, Leiman & Breedlove, 1999).

Abnormalities of dopam ine function in schizophrenia are suggested by the antidopaminergic properties of antipsychotic medications (Laruelle & Abi - Dargham, 1999). For example, conventional neuroleptics (e.g. chlorpromazine, Haloperidol), which are dopamine antagonists, act by blocking postsynaptic dopamine D2 receptors in the mesolimbic area and facilitate the reduction of positive symptoms in some individuals (Provencher, Fournier & Dupuis, 1997). Conversely, acute side effects result from drugs that exert their effects on dopa mine systems, but subsequently provide further support for the dopamine hypothesis. For example, Tardive Dyskinesia, characterised by an abnormality of movement control similar to those seen in Parkinson's disease (Harrison, 1999), is thought to result from an oversensitivity of dopamine

receptors, caused by a compensatory response to the dopamine inhibiting effects of neuroleptics. In Parkinson's disease, the dopamine containing neurons in the substantia - nigra degenerate. The symptoms of the disease are b rought on by the consequent decrease in of dopamine transmission in the basal ganglia. Treating patients with L -Dopa (which converts to dopamine in the brain) reduces Parkinsonian symptoms, but exacerbates 'schizophrenia - like' symptoms (Thompson, 2000), thereby suggesting that increased levels of dopamine exacerbate schizophrenia symptoms.

In addition, further support for the dopamine hypothesis comes from the observation that dopamine agonists (e.g. amphetamines), that increase dopamine activity in the brain by blocking dopamine re-uptake, produce symptoms similar to the positive symptoms of schizophrenia (Carter, 1998). However, this hypothesis has undergone challenges and adjustments in recent years (Schwartz, 1999, as cited in Comer, 2001) as research has shown that the production and release of dopamine in the brains of schizophrenics is not always abnormal (e.g. Wyatt, Kirch & DeLisi, 1988, as cited in Carlson, 1991). Furthermore, post -mortems carried out on schizophrenics have found their brains to contain an unusually large number of dopamine receptors, leading researchers to propose that over -sensitivity of dopamine receptors, not high levels of dopamine, could be implicated in the positive symptoms of schizophrenia (Kwak, Koo, Choi & Sunwoo, 2001). However, increased density of D2 receptors, reported in most post mortem studies, has been difficult to interpret, given that neuroleptic drugs up -regulate these receptors (Powchik, Davidson, Haroutunian et al., 1998). Further studies are needed to establish whether abnormal amounts of receptors are present in antipsychotic naïve patients.

Furthermore, although the importance of dopamine in schizophrenia is not disputed, it is by no means the whole story, for example, neuroleptics bind to dopamine receptors rapidly, but clinical improvement develops slowly, therefore suggesting that neuroleptics may affect other neurotransmitters. Consistent with this, there is compelling evidence from recent studies that increased dopaminergic indices in schizophrenia m ight indicate that dopamine transmission is only enhanced relative to other systems, such as the glutaminergic system (e.g. Akhondzadeh, 1998) and/or the serotoninergic system (e.g. Bantick, Deakin & Grasby, 2001). For example, several atypical anti-psychotic medications (e.g. Clozapine and Risperidone) exert their therapeutic effects by blocking dopamine and serotoninergic receptors (Warner, 1999). Serotonin is known to inhibit dopaminergic neurons, therefore, blocking both may regulate dopamine to within 'normal' levels, furthermore, drugs that block only serotonin (5 HT2) receptors do not demonstrate efficacy in the treatment of psychosis (Thompson, 2000). To this end, schizophrenia symptoms could be related to an interaction of both dopamine and serotonin receptors, and not just increased dopamine levels (Comer, 2001).

Still another suggestion is that changes in dopamine levels are secondary consequences of a loss of glutaminergic stimulation (Rosenzweig et al., 1999). Glutamate is an excitatory neurotransmitter that is widespread in the brain. Phencyclidine (PCP), which blocks the NMDA glutamate receptor, produces a syndrome closely resembling schizophrenia, including positive and negative symptoms and cognitive impairment (Akhondzadeh, 1998; Noorbala & Akhondzadeh et al., 1999). Furthermore, administrations of NMDA antagonists, such as chlorpromazine, which are dopamine agonists, enhance the function of NMDA and reduce negative symptoms (Do, Trabesinger, Kirsten-Kruger et al., 2000). Because one action o f dopamine receptors is to inhibit glutamate release, a primary defect in the dopamine system that causes dopamine hyperactivity (and subsequent positive symptoms) could result in excessive suppression of glutamate release at NMDA receptors, with consequential hypofunction of the NMDA receptor systems (Akhondzadeh, 1998). This again suggests a possible interaction of several neurotransmitters, including dopamine, as possible causal factors in schizophrenia symptoms, particularly the positive symptoms, which are posited to be a product of dopamine dysfunction within the brain (Warner, 1999). These pharmacological effects suggest, but do not establish, a dysregulation of dopamine systems in schizophrenia. Nonetheless, they could offer an explanation as to why both positive and negative symptoms are sometimes seen in the same individual (Laruelle & Abi - Dargham, 1999). To this end, it could be suggested that dopamine

hyperactivity seems to lead to the positive symptoms of schizophrenia, and dopamine under activity to the negative symptoms, therefore, there seems to be inverse levels of cortical -sub cortical dopaminergic function (Harrison, 1999).

Despite the extensive evidence in support of the dopamine hypothesis, other characteristics have been identified that distinguish schizophrenics from controls. For instance, several recent major reviews and studies in leading journals on the neuropathology of schizophrenia have highlighted alterations or abnormalities in the brains of schizophrenia patients (Halliday, 2 001). Evidence from computerised tomography (CT) scans and magnetic resonance imaging (MRI) studies suggest that a percentage of schizophrenics, particularly those with chronic, negative symptoms (e.g. poverty of speech or loss of drive), have an enlargement of the lateral ventricles (e.g. Giedd, Jeffries, Blumenthal et al., 1999). This suggests a deterioration or atrophy of brain tissue in adjacent areas, such as the hippocampus and amygdala (Scarr, Copolov & Dean, 2001). A study of monozygotic twins disco rdant for schizophrenia provided clear evidence for a ventricular enlargement in schizophrenia, showing that the ventricles of the schizophrenic twin were enlarged, whereas the 'normal' twin showed no enlargement (Torrey, Bowler, Taylor & Gottesman, 1994, as cited in Rosenzweig et al., 1999). In addition, studies of the limbic system (e.g. hippocampus, amygdala and parahippocampal regions) in schizophrenic patients have observed size differences in the hippocampus of chronic schizophrenics when compared to controls (Rajarethinam, Dequardo, Mielder et al., 2001). The hippocampus is suggested to play an important role in learning (Thompson, 2000). A disorganisation of neurons within the hippocampus, which is linked to the mesolimbic pathway, may cause problems for an individual attempting to make sense of their environment (Scarr, Copolov & Dean, 2001). It makes intuitive sense, therefore, to focus on this area when investigating disorders of association in schizophrenia.

The frontal lobes are involved in hig her executive functioning, such as motor function, problem solving, spontaneity, memory, language, and social behaviour, and have been implicated as important in the negative symptoms of schizophrenia (Carter, 1998). Low frontal activation (hypofrontality) is related to the severity of negative symptoms, with many studies observing the association between negative symptoms and decreased frontal cortical blood flow (e.g. Wible, Anderson, Shenton et al., 2001). A common test for frontal lobe function is the Wisconsin Card Sorting Task (WCST). This was employed by Zhening, Wai-Cheong, Yaning & Jingping (2002) to explore the relationship between regional cerebral blood flow (rCBF) and problem solving in negative symptom schizophrenics. 21 patients and 12 normal controls were studied using single photon emission computed tomography (SPECT). Measures of rCBF were taking both at rest and during a prefrontal activation task (WCST). Compared with controls, poor performances were found in the schizophrenia patients, w ho showed a significantly lower rCBF rate in the prefrontal lobe during the WCST than controls. They conclude that schizophrenic patients with negative symptoms have executive function deficits and lower rCBF perfusion in left prefrontal lobes, a finding which is widely supported (e.g. Esel, Kula, Gonul et al., 2000).

Recent explanations for the symptoms of schizophrenia (e.g. Davis, Kahn & Davidson, 1991, as cited in Laruelle & Abi- Dargham, 1999) have converged to suggest although both positive and negative symptoms have different origins, both may be linked to dopamine. The negative symptoms, although primarily due to brain structure abnormality, may be caused by a lack of dopaminergic input into the frontal lobes, which subsequently may effect dopamine levels in the limbic system because both are connected via the mesolimbic pathway (Thompson, 2000). Because of the underactivity in the frontal lobes, the limbic system may be under stimulated which is then compensated for by increasing sensitivity to sti muli which would normally be ignored. This could lead to delusions and hallucinations, which are implicated in the positive

symptoms of schizophrenia (Chua & McKenna, 1995). Negative symptoms could be explained in terms of dopamine deficit in frontal lobes. Characteristically, individuals with predominately negative symptoms show deficits that could be explaining by higher executive function deficits (e.g. flattened emotional response, poverty of speech etc.), therefore, all of these symptoms could originate from a lack of dopamine in this area (Potkin, Alva, Fleming et al., 2002). Andreasen (1994) sums this all up quite nicely, stating, …"A crucial question is one of the irreversibility of negative symptoms. If they were truly irreversible, this would strongly support the view that their etiological basis is cell loss - once a given structure in the brain is lost, its function cannot be retrieved. Pharmacological control of negative symptoms, on the other hand, would imply the causation is neurochemical at le ast in the treatable cases, while leaving the possibility of mixed causation open" (as cited in Leonard, 1997, p. 245).

To conclude, due to the heterogeneity of schizophrenia, any theory provides only a limited explanation, however, biological theories, such as biochemical, structural and functional brain abnormalities go a long way in explaining both the positive symptoms and negative symptoms of schizophrenia. However, to focus on biological theories alone, as an explanation for schizophrenic symptoms, is to take a very narrow view, as individuals do not develop or live in isolation, and thus, any explanations offered must address all perspectives and subsequent theories of the development and maintenance of positive and negative symptoms. It could therefore be suggested that individuals with some form of brain dysfunction may be more likely to be affected by stressful situations (e.g. Norman & Malla, 2001), and consequently develop the symptoms of schizophrenia, however, further research is needed in this area. It can be concluded, from the evidence put forward, that structural or functional brain abnormality as a primary factor, coupled with increased or decreased neurotransmitter dysfunction do provide an adequate explanation for both the positive and negative symptoms of schizophrenia.