The influence of social support and oxytocin on health outcome

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Abstract

In this review the association between social support and health was examined. The influence of social support on health has been suggested to be mediated by the neuropeptide oxytocin. In this thesis is examined what the role of oxytocin is in the association between social support and health. A literature search in Pubmed delivered 12 articles from which 6 discussed the influence of oxytocin on the HPA axis, 4 articles discussed the influence of oxytocin on the SAM axis, 1 article discussed both the HPA axis and the SAM axis, and 1 article discussed a possible influence of oxytocin on the immune system. The findings indicate a suppressing influence of oxytocin on the SAM axis and the HPA axis, which leads to beneficial health outcome. One single study showed the positive influence of oxytocin on the immune system. Recommendations were made according to future research on the role of oxytocin in social support.

Keywords: HPA axis, SAM axis, oxytocin, health, social support.
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**Introduction**

Social interactions shape people from early development throughout old age and have a great influence on many aspects of physiology and behaviour. They are essential for proper cognitive, affective and behavioural development. There are different kinds of (social) support, and it can be subdivided into emotional, instrumental (functional) and informational support (Karelina, 2011). Emotional support is the offering of love, trust, empathy, caring etc. (Langford et al., 1997; Slevin et al., 1996). It is the warmth provided by the sources of social support (Taylor, 2011). Instrumental support is the provision of financial material, goods, services etc. (Heany & Israel, 2008). This kind of social support encompasses the concrete, direct way people assist others (Langford et al., 1997). Informational support means providing someone advice, solutions, guidance, useful information etc. (Wills, 1991; Krause, 1986). This type of support can help the other solve problems (Tilden & Weinert, 1987; Langford et al., 1997).

Many studies have suggested that positive social support improves patient recovery from diseases with an inflammatory component (Barry et al., 2006; Cohen et al., 2007; Seeman et al., 2000; Strating et al., 2006). Particularly in chronic disease states, the benefits of social support are salient, while loneliness and social isolation can have detrimental effects on mental and physical health (Arora et al., 2007).

Social support seems to improve health by promoting health behaviours. It is associated with better medical compliance, increased physical exercise, improved nutrition, and low-to-moderate tobacco and alcohol consumption. Furthermore, social and peer support increases the likelihood of engaging in health behaviours (Cohen & Lemay, 2007).

On the other hand, a physiological explanation for the role of social support in health includes the biochemical oxytocin. Oxytocin is a neuropeptide that is released, among others, during social interactions. It plays an important role in mother-infant bonding, partner-partner bonding, but is also released in other social situations. Exogenous oxytocin administration has been shown to increase prosocial behaviours in human, including the ability to interpret emotions of others, interpersonal communication, and social approach behaviour (Shamay-Tsoory et al., 2009).

Oxytocin is produced in high concentrations in the supraoptic and paraventricular nuclei of the hypothalamus, which in turn project to the posterior pituitary, which releases oxytocin. Oxytocin released to the blood circulation subsequently reaches its central and peripheral targets (Karelina et al., 2011). However, oxytocin can also act as a neurotransmitter.
The biological activity of oxytocin is mainly mediated by the oxytocin receptor. Brain structures like the hypothalamus and amygdala are suggested targets for the onset and maintenance of the effects of oxytocin on social behaviour (Karelina et al., 2011).

Several animal studies have investigated the influence of oxytocin on social behaviour. These studies have shown both causal and regulatory roles for oxytocin in the context of animal social behaviour. The effects of social interaction on health can be examined using animal models, mostly rodents. Prairie voles are rodents, which are interesting animals to investigate the differences between the kinds of social bonding. Difference between the ‘prairie vole’ and the ‘meadow vole’ for example is that the one is monogamous and the other more social (Young et al., 2008; 2011). These animal models show that socially housed and socially isolated animals have quantitatively and qualitatively different pathophysiological responses to injury (Karelina et al., 2011). Considering this information, it can be hypothesized that oxytocin acts as a mediator in the association between social behaviour and health outcomes.

It is interesting to examine how oxytocin influences health, and which physical mechanisms are involved. According to literature there is a positive influence of oxytocin on health in stressful situations (e.g. Taylor, 2006); oxytocin modulates the stress response. It is interesting to examine, how the stress response is modulated.

Two stress regulating mechanisms are the HPA axis and the SAM axis. HPA stands for hypothalamus-pituitary-adrenal axis. In this system cortisol is periodically released (Sapolsky et al., 2000). When a person experiences stress, the hypothalamus releases corticotrophin releasing factor which reaches the pituitary. In turn, the pituitary releases adrenocorticotrophin releasing hormone (ACTH). ACTH goes to the adrenals, which release cortisol (a glucocorticoid from the adrenal cortex). When there is sufficient cortisol in the blood (or too much of it), negative feedback is sent to the hypothalamus or the pituitary. This negative feedback allows the body to respond to acute energetic demand and minimizes long-term exposure to high concentrations of corticosteroids (Sapolsky et al., 2000). Therefore, negative feedback results in inhibiting the release of CRF, ACTH and cortisol.

Sufficient amounts of cortisol, prevent the detrimental effects of stress (Le Moal & Mayo, 2002). The release of cortisol results in increased blood glucose, cortisol acts immunosuppressant and it dampens stress response (the negative feedback, early mentioned). Chronic high levels of cortisol are detrimental, because in contrast to acute stress response, a chronic stress response suppresses the immune system response.
Another stress regulating mechanism is the SAM axis. SAM stands for sympathetic-adrenal-medullary. The main hormones involved in this system are adrenaline and noradrenaline. The SAM axis becomes activated when a person experiences (immediate) stress. Consequently, the adrenal medullary releases adrenaline or noradrenaline (Padgett & Glaser, 2003). When adrenaline is released the person feels excited and the following physical changes can occur: increase in blood pressure, increase in heart rate- and beat, the blood goes from the skin and the viscera to the skeletal muscles, coronary arteries, liver and brain (the person looks pale), a rise in blood sugar (for enough energy), the bronchi dilate (the uptake of oxygen increases), the pupils dilate, hairs stands on (gooseflesh), reduction of clothing time of the blood and increased ACTH secretion from the anterior lobe of the pituitary (Padgett & Glaser, 2003).

Oxytocin modulates the stress response, therefore, it can be expected that it influences the HPA axis and the SAM axis. Chronic high levels of cortisol and other stress hormones have detrimental effects on the immune system, so a negative influence on health. It is interesting to examine how the HPA axis and the SAM axis are influenced by oxytocin.

The main research question in the present review is: How does oxytocin mediate the association between social support/behaviour and health? How are the SAM axis and the HPA axis influenced in this process?
Method

In order to examine the research questions in this thesis, a search for scientific articles was done in Pubmed.

The main research question in this thesis is: How does oxytocin mediate the association between social support/behaviour and health? The search terms used in Pubmed to find literature for answering the question, have come in practice as described below.

Search terms
The (MeSH) search terms for the search session were the following: ("Social Distance"[Mesh] OR "Social Support"[Mesh] OR "Social Isolation"[Mesh] OR "Social Behaviour"[Mesh]) OR “social stress” OR "Social Dominance"[Mesh]. Furthermore, the term ‘loneliness’ was added.

Furthermore, the term ‘oxytocin’ was combined and factors like ‘pregnancy’ or ‘birth’ or ‘labour’ were excluded and using only human studies. Eventually, the following search terms were used: ("Social Distance"[Mesh] OR "Social Support"[Mesh] OR "Social Isolation"[Mesh] OR "Social Behaviour"[Mesh]) OR “social stress” OR "Social Dominance"[Mesh] OR loneliness) AND oxytocin NOT (pregnancy OR labour OR birth) AND human. Next, the term ‘health’ was added to the search and the following terms resulted: ("Social Distance"[Mesh] OR "Social Support"[Mesh] OR "Social Isolation"[Mesh] OR "Social Behaviour"[Mesh]) OR “social stress” OR "Social Dominance"[Mesh] OR loneliness) AND oxytocin NOT (pregnancy OR labour OR birth) AND human AND health (41 hits).

The screening of the 41 articles delivered 11 relevant articles. A reference search of the 11 articles, delivered one extra article: the article of Kirschbaum and colleagues (1995), was retrieved by the reference list of the article from Heinrichs and colleagues (2008).
Inclusion criteria

Articles were included when they described the role of oxytocin in the association between social support and health.

Exclusion criteria

Articles with other themes like protocols about oxytocin administration, oxytocin in relation to some psychiatric disorders and articles with other not relevant themes, were excluded. Furthermore, those studies that described the relation between social support and health without the mediating role of oxytocin, were excluded.
Results

From the 12 articles, 6 articles studied the influence of oxytocin on the HPA axis, 4 articles studied the influence of oxytocin on the SAM axis, and 1 review was both on the HPA axis and SAM axis. Finally, 1 article studied the role of oxytocin in the immune system.

The first part in this results section is about the role of oxytocin on the HPA axis. The second part is about the role of oxytocin on the SAM axis. Finally, 1 study is discussed, to explain the role of oxytocin on the immune system.

Oxytocin and HPA axis

2 comparable studies found similar results on the role of oxytocin and social support on cortisol levels in plasma. Heinrichs, Baumgartner, Kirschbaum and Ehlert (2003) did a placebo-controlled, double-blind study in which 37 healthy men were exposed to a Trier Social Stress Test. The participants were randomly assigned to receive intranasal oxytocin or placebo 50 minutes prior to stress (speech). During the preparation period they either received social support from their best friend or no social support. Participants who received emotional and instrumental support and oxytocin administration prior to social stress, exhibited lower cortisol levels compared to people who did not receive social support and a placebo.

A comparable study was done by Kirschbaum, Klauer, Filipp and Hellhammer (1995). They investigated the effect of short-term social support on cortisol levels and subjective responses to acute psychological stress (Trier Social Stress Test) in adults (N=66). 32 men and 34 women were randomly assigned in one of the 3 experimental groups: Group 1: no social support (N=23); Group 2: social support provided by a stranger (N=22); Group 3: social support provided by the subject’s boyfriend or girlfriend (N=21). Support providers were instructed to enact both instrumental and emotional support in the anticipation period. Results suggested sex-specific effects of social support. Although men in the partner support condition showed significant attenuation of cortisol responses compared with unsupported and stranger-supported men, women showed no response decrement under stranger support. In contrast to men, women showed a tendency toward increased cortisol responses when supported by their boyfriends.

Both studies suggested a suppressing influence of social support and oxytocin on the HPA axis. The study of Kirschbaum and colleagues revealed sex-differences in cortisol response due to different support providers.
Oxytocin has an influence on the HPA axis in stressful situations. The review of De Vries, Glasper and Detillion (2003) and Carter (1998) reveal a recurrent association between high levels of HPA axis activity and the subsequent expression of social behaviours and attachments. Positive social behaviours, including social bonds, reduce HPA axis activity, while in some cases negative social interactions can have the opposite effect. Both oxytocin and social interaction seem to reduce HPA axis activity, perhaps accounting for health benefits that are attributed to loving relationships (Carter, 1998). According to De Vries and colleagues (2003), the potential mechanism through which the corticosteroids are suppressed, is oxytocin-induced. This conclusion was based on the finding that lactation prevents stress induced increases in CRF mRNA (Lightman and Young, 1989) and that cortisol does not increase (in men) treated with exogenous oxytocin (Legros, Chiodera and Greenen, 1988).

The suppression of the HPA axis is done on the level of the pituitary and on adrenal level. Beside its hypophysial inhibitory action on ACTH release, oxytocin acts also at the adrenal gland level to decrease cortisol release and/or synthesis in normal human subjects (Legros et al., 1988).

Wound healing is a research model, which enables scientists to investigate how the healing of the wound is compromised. There are three general stages of wound healing in humans and other animals: an inflammatory stage; a proliferative stage; and a remodelling stage. Restriction stress (i.e. immobilization) in rodents affects the early inflammatory stage by reducing the cellular infiltration of leukocytes (i.e. macrophages), the source of proinflammatory cytokines, to the site of the wound (Padgett, Marucha and Sheridan, 1998).

Detillion, Craft, Glasper, Prendergast and de Vries (2004) did a study to determine, whether positive social interaction, which is known to influence HPA axis activity in social rodents (Young, Gobrogge, Liu and Wang, 2011), promotes wound healing. Furthermore, a part of the review of Ishak, Kahlloon and Fakhry (2011) also discussed the wound healing research model.

In the study of Detillion and colleagues (2004), Siberian hamsters received a cutaneous wound and were then exposed to immobilization stress. Chronic restraint stress reduces cutaneous wound cellularity and delays wound closure, an effect likely mediated by stress-induced increases in circulating glucocorticoid concentrations (Padgett et al., 1998). The results showed, that stress increased cortisol concentrations and impaired wound healing in isolated, but not in socially housed hamsters. Detillion and colleagues (2004) also injected the experimental hamsters with oxytocin, once a day during five days prior to the restraint
stress. The administrated oxytocin blocked stress-induced increases in cortisol concentrations and facilitated wound healing, compared to the control group injected with saline. Treating them with an oxytocin antagonist delayed wound healing. Comparable results are discussed in the review of Ishak and colleagues (2011). Their most important finding was that oxytocin administration results in lowering of cortisol level and thus improves wound healing and inflammation. Subjects with low oxytocin levels would be more prone to poor wound healing and pro inflammatory states.

The study of Detillion and colleagues and the review of Ishak and colleagues (2011) both showed the beneficial influence of social support on wound healing. Social support and oxytocin administration reduce the stress response and prevent the increase of cortisol concentrations, which facilitates wound healing.

Data reviewed by Knox and Uvnäs-Moberg (1998), suggest that lack of social support is etiologically related to coronary artery development through the mechanisms of HPA axis and SAM axis. The SAM axis will be explained in the next section, in this part an explanation will be given about how the HPA axis is related to the coronary artery development. Before the role of the HPA axis is discussed, the process of coronary artery development will be explained. The explanation is a summary of the findings of Ross (1993a; 1993b).

After injury to the endothelium (layer of epithelial cells that line the lumina of blood vessels), there comes a change in its function and or structure, so that adhesive glycoprotein’s begin to attach to it. T lymphocytes and monocytes attach to these glycoproteins and are then actively moved into the subendothelial matrix. This process (chemotaxis) is facilitated by growth regularly molecules and chemotactic factors. The monocytes differentiate to macrophages, and by ingestion of lipids become foam cells. These foam cells form fatty streaks, after accumulating together with the lymphocytes. This process is followed by smooth cell (e.g. blood vessels contain smooth cells) proliferation, which is regulated by a number of cytokines and growth factors. The lesion progresses by adding more layers of foam cells and smooth muscle cells (Ross, 1993a; Ross 1993b).

Pituitary-adrenal cortical factors are involved in smooth cell proliferation during progression of the lesion, after injury has taken place (Knox and Uvnäs-Moberg, 1998). Pituitary factors are necessary for smooth muscle cell proliferation to occur (Fingerle et al., 1992). Study on hypophysectomised rats (rats from which the pituitary gland is removed by surgery), showed that muscle cells will not proliferate in response to injury in animals without a pituitary (Fingerle et al., 1992). This means that the activation of the HPA axis stimulates the
progression of coronary artery disease. Due to pituitary-adrenal cortical factors released during the activation of the HPA axis, the accumulation of the foam cells gets stimulated. The suppression of the HPA axis by oxytocin results in the inhibition of the pituitary-adrenal factors, so the progression of coronary artery disease is prevented.

The previous studies and reviews suggest that social support is *in any case* beneficial in stressful situations, through its suppressing working on the HPA axis. The process of wound healing is promoted by oxytocin release. Furthermore, pituitary factors are necessary for smooth muscle cell proliferation to occur. Oxytocin suppresses the HPA axis and thereby slows the coronary artery development. [Niet helemaal duidelijk wat bevindingen zijn en wat beredeneerd is, bijv. bij CAD risk]

**Oxytocin and SAM axis**

A second system hypothesized to affect the relation of oxytocin on health is the SAM axis. First two comparable studies are described, which examine the association between oxytocin and stress hormones and blood pressure as a response to warm touch support. The studies are done by Grewen, Girdler, Amico and Light (2005) and Holt-Lunstad, Birmingham and Light (2008).

Grewen and colleagues (2005) examined whether the magnitude of plasma oxytocin, norepinephrine, cortisol, and blood pressure responses before and after a brief episode of warm contact with (cohabiting) spouse/partner would be related to the strength of perceived partner support levels. They found that greater partner support (based on self-report) was associated with higher plasma oxytocin in men and woman across the protocol before and after warm contact. Furthermore, in women, greater partner support was correlated with lower systolic blood pressure during solitary rest after, but not before warm contact. In addition, higher oxytocin at baseline (before the oxytocin administration in the following 3 measure moments) in woman was linked to lower blood pressure at baseline and to lower norepinephrine at all measurements. Both men and women who reported greater support from their partners showed higher plasma oxytocin levels when resting alone both before and after a period of warm physical and emotional contact.

The study of Grewen and colleagues (2005) demonstrates an association between
oxytocin and a decrease in blood pressure and with lower levels of norepinephrine. Enhanced oxytocinergic activity inhibits the sympathetic nervous activity. However, it should be noted that the effect of oxytocin was only found in women. The authors explained, that the greater cardiovascular effects of oxytocin linked to partner support in women, was perhaps the result of the enhancing influence of estrogen on oxytocin activity, availability and receptor binding. Grewen and colleagues (2005) did not control for this effect of estrogen.

However, the cardiovascular effects of oxytocin seem also to be present in men. Holt-Lunstad and colleagues (2008) investigated whether warm touch enhancement influenced physiological stress systems that are linked to important health outcomes. Healthy married couples were randomly assigned to a ‘behavioral monitoring’ control group or participated in a 4-week intervention study. The intervention couples received instructions according to Couple Contact Enhancement Techniques. A male and female staff member led the couples through the examples of the Couple Contact Enhancement Techniques.

Clinical levels of plasma oxytocin (immediate single-stick venipuncture five minutes after warm contact), 24-hour ambulatory blood pressure, and salivary cortisol and alpha amylase were obtained pre and post intervention, at the same time salivary oxytocin was taken at home during one and four weeks. The results showed that salivary oxytocin was enhanced both early and late in the intervention group. Husbands in the intervention group had significantly lower post treatment 24-hour systolic blood pressure than the husbands in the control group. The effect of intervention on systolic blood pressure, was greater for husbands than wives. This could be explained by the fact that the pre-treatment blood pressure of women was quite low, compared to the higher blood pressure of the husbands, which may have caused the floor effect (Holt-Lunstad et al., 2008).

To examine the action of the SAM axis, studies are done in prairie voles (e.g. Grippo, Trahanas, Zimmerman, Porges and Carter, 2009). Grippo and colleagues (2009) did a study in which adult prairie voles were exposed to social isolation or continued pairing with a sibling (this was the control condition) for 4 weeks. During weeks 3 and 4, these animals were administrated oxytocin or saline vehicle, daily for a total of 14 days.

There were 2 experiments. In experiment 1, measuring of autonomic parameters occurred during and following isolation or pairing. Isolation significantly increased basal heart rate and reduced heart rate variability and vagal regulation of the heart. These physical
changes refer to SAM axis activity. The results showed that these changes in the isolated prairie voles were prevented with oxytocin administration (Grippo et al., 2009). The results of Grippo and colleagues (2009) are consistent with the studies discussed previously.

In the 2nd experiment, behaviors relevant to depression were measured as a function of isolation. These depressed behaviors included sucrose intake and swimming in the forced swimming test. A decrease in sucrose intake compared to baseline levels, and immobility during the forced swimming test were seen as indicators of depression. Sucrose intake was reduced, and immobility increased in the forced swim test in the prairie voles which were socially isolated. These behaviors in isolated prairie voles were prevented by oxytocin administration.

The findings of Grippo and colleagues (2009), clearly support the suggestion that oxytocinergic mechanisms can protect against behavioral and cardiac dysfunction in response to chronical social stressors.

The studies of Grewen and colleagues (2005), Holt-Lunstad and colleagues (2008) and Grippo and colleagues (2009) show the suppressing influence of oxytocin on the SAM axis activity. In the review of Knox and Uvnäs-Moberg (1998) the beneficial influence of oxytocin is discussed in artherosclerosis.

Knox and Uvnäs-Moberg (1998) pointed to a link between the SAM axis and atherosclerosis. In their review they discussed findings from Kaplan, Pettersson, Manuck and Olsson (1991). Kaplan and colleagues (1991) summarized some separate experiments to show the link between the SAM axis and atherosclerosis. These experiments were performed on cynomolgus monkeys (Macaca fascicularis), whose cardiovascular systems shows resemblance to that of humans.

In a set of experiments, specific mechanisms were examined. The first tested the effect of treating one group of monkeys in a socially unstable environment with propranolol HCL (a b-adrenergic blocker) on a daily basis for the 2 years of the experiment; the other group was left untreated. In the monkeys treated with the b-blocker, there was a significant reduction of heart rate and blood pressure. In the treated dominant monkeys, there was significantly less coronary artery atherosclerosis than in the dominant untreated monkeys. These data indicate a b-adrenergic influence on lesion formation in a subset of monkeys (dominants) in a chronically stressful situation. B-adrenergic blockers inhibit sympathetic nervous system function. Therefore, it can be hypothesized that there is an influence of the SAM axis on
lesion formation. Comparable results were described in other experiments of Kaplan and colleagues (1991).

Kaplan and colleagues (1991) suggested a sympathetic system role on platelet formation and lesion formation. The use of b-blockers which dampens the action of the sympathetic nervous system, prevented or decreased the deleterious effects of the sympathetic nervous system on cell death and lesion. In the same way, oxytocin can dampen the action of the SAM axis. Oxytocin somehow mimics the action of b-blockers, by binding the receptors found in the SAM axis system. SAM axis activation seems to be associated with both lesion formation and endothelial dysfunction. Both of these can be affected by chronic stress (Knox and Uvnäs-Moberg, 1998). When a person receives support (increase in oxytocin release), a reduction occurs in the cardiovascular reactivity to acute stress. Oxytocin release and its administration can induce sedation, lowering of pulse rate and blood pressure (Uvnas-Moberg, 1997). In the same way, ongoing lack of social support (reduction of oxytocin release) is associated with increased resting levels of sympathetic activation, which means that lack of social support itself is a stressor (Knox and Uvnäs-Moberg, 1998).

So far, the HPA axis and the SAM axis are discussed. In the next part the role of oxytocin will be discussed in the immune system.

**Oxytocin and the immune system**

Fekete and colleagues (2011) examined circulating levels of plasma oxytocin as a moderator of the effects of stress on disease status (viral load, CD4+ cells count) in low-income ethnic minority women with HIV disease. Stress was measured by the 14-item Perceived Stress Scale and the number of stressful life events was measured by the Difficult Life Circumstances Questionnaire. Oxytocin, viral load and CD4+ cell counts were measured using plasma collected through morning peripheral venous blood samples.

Fekete and colleagues (2011) found an inverse association between stress and CD4+ cell counts. This was not a surprising finding, because stress has a negative influence on the immune system. A counter-intuitive finding was that at high levels of oxytocin there was a positive association between stress and CD4+ cell counts. This is counter-intuitive because
one expects that high levels of stress would have a negative effect on the immune system, so the CD4+ cell counts should decrease. However, there is an opposite effect. The positive effect is due to high levels of oxytocin which means that through any mechanism oxytocin ameliorates CD4+ cell counts in times of stress. The presence of high levels of circulating oxytocin may act as a buffer against the negative effects of stress on immune status in low income minority women with HIV. However, the amounts of viral HIV cells were nor decreased nor increased as result of the positive association between stress and CD4+ cell counts in relation to oxytocin.

Furthermore, Fekete and colleagues (2011) did not report down-regulation of other neuroendocrine hormones known to do so (cortisol, norepinephrine); thus, the interactive effects of perceived stress/stressful life events and oxytocin on CD4+ cell count in the sample of low income minority women with HIV were not mediated by women’s HPA and SAM urinary hormone levels. The authors explained the association found in the study, by considering the ability of oxytocin to enhance immune systems directly.
Discussion

In this thesis the role of oxytocin in the association between social support and health was examined. The main research question was: How does oxytocin mediate the association between social support/behaviour and health? Hereby the following sub question was formulated: How are the SAM axis and the HPA axis influenced in this process? To answer the research questions, a literature search was done in Pubmed.

The results consistently showed that the HPA axis and the SAM axis are important mechanisms through which oxytocin influences health. That is, the HPA axis and the SAM axis are suppressed/inhibited by oxytocin. The evidence comes both from animal and human studies.

In addition, one study investigated the role of oxytocin on the immune system. Because there was no down-regulation of the hormones of the HPA axis and the SAM axis, one can argue that oxytocin ameliorates CD4+ cell counts through any other mechanism. It can be suggested that oxytocin has the ability to enhance immune systems directly. Yet, the role of oxytocin on the immune system should be further examined, because in this thesis just one study has been discussed. Furthermore, the study of Fekete and colleagues (2011) was conducted in women with HIV and a low income, which can not be generalised to other diseases with other immune conditions. However, the study is a successful attempt to examine the influence of oxytocin on the immune system.

From the results it can be concluded that social support (high levels of oxytocin) has a positive influence on health, by reducing stress hormones and cardiovascular reactivity. The important role of the SAM axis on platelet formation, and the HPA axis on smooth cell proliferation was already discussed in the review of Knox and Uvnäs-Moberg (1998). Both stress mechanisms stimulate the process of coronary artery development, which implicates a negative influence on health. Therefore, people at risk of coronary artery development should be cautious and avoid loneliness, and try to use the beneficial effects of social support.

Moreover, in the explanation of coronary artery development, the role of immune system factors like macrophages, lymphocytes, cytokines and growth factors was explained. It is clear that the HPA axis and SAM axis interact with the immune system to influence coronary artery development. More research is necessary to find additional ways through which the two
stress mechanisms and the immune system interact. The role of oxytocin will be important in here, because of the possible direct positive influence of the neuropeptide on the immune system. The mechanism through which oxytocin influences the immune system, may contain oxytocin receptors. Further research can examine this.

The results section showed the beneficial role of oxytocin in people without any social impairments. The articles studied the role of oxytocin in people from which the brains have a normal regulation of oxytocin. In some psychiatric disorders (e.g. autism), people suffer from social impairments. Oxytocin regulation in the brains of people with autism is different compared to control groups (e.g. Green and Hollander, 2010). Therefore, the possibility exists that these people do not benefit from the positive effects of oxytocin on health. Important to note, according to Green and Hollander (2010), the difference in regulation of oxytocin in the brains of people with autism and controls, does not mean that people with autism have reduced levels of oxytocin release. In an adult population, autism spectrum disorder patients had higher oxytocin plasma levels than control subjects (Jansen et al., 2006). To account for this, it has been suggested that oxytocin is processed differently in the brains of autism spectrum disorder patients, rather than simply at a different level (Green et al., 2006). It may be interesting to examine how people with autism spectrum disorder physiologically react to social support (oxytocin release), compared to people without this disorder. It can be hypothesized that people with autism have a worse health outcome, compared to people without autism, because of the social impairment. Further research can examine this. In addition, a study of Cysneiros and colleagues (2009) suggested that the anti-psychotics taken by patients suffering from autism, contain side effects which can lead to cardiovascular problems and even cardiac death. They found that the side effects could be decreased by taking omega-3 fatty acids supplementation cardiovascular problems. Social support and oxytocin release may have the same effect on health in people with autism spectrum disorder. Further research can examine this.

A critic point in this thesis is that to examine the role of social support on health, the broad term ‘social support’ was used, without making a distinction between the different kinds. As explained in the introduction, there are different kinds of social support. Karelina and colleagues (2011) made the distinction between emotional, instrumental and informational support. It could be that the different kinds of support are experienced in a different way. Consequently, this differential experiencing can result in differential amounts of oxytocin release. Therefore, it should be investigated whether the health outcome effects of oxytocin
are different for different kinds of social support. Important to note, ‘warm touch’ support (Holt-Lunstad et al., 2008), affiliative behaviour and ‘verbal support from a close long-term friend’ (Kirschbaum et al., 1995) are associated with low levels of cortisol, decrease in blood pressure and decrease in heart rate. These kinds of support do indicate emotional support. Berkman and colleagues (1995) asserted that for social support to have the greatest health benefits, it must engender feelings of intimacy and belonging. Therefore, it can be argued that emotional support has a beneficial influence on health, whereby the SAM axis and HPA axis are suppressed/inhibited by oxytocin.

Instrumental support may also have the suppressing effect on the HPA axis. This suppressing effect was found in the experiment of Heinrichs and colleagues (2003), in which emotional and instrumental support were associated with low cortisol levels. However, instrumental and emotional support was examined simultaneously. Therefore, the possibility exists that the low cortisol levels were mainly due to emotional support.

In the other cases only broad terms like ‘social support’ and ‘social interactions’ were used, which were examined in association with health. Social support may have been emotional or instrumental here, but no exact descriptions (of emotional or instrumental support) were given. Further research should specify the separate kinds of support, and examine how the different kinds are related to oxytocin release.

One of the limitations in this review is that the results are partly derived from reviews, especially, the results on the HPA axis. In reviews, authors choose studies which seem relevant to them, and mostly give their own interpretation on it. In this thesis it has been tried to avoid the own interpretations of the review authors, and to focus on the descriptions of the single studies given in those reviews.

A second limitation is that a small number of relevant articles are found to answer the research question. However, all the articles give the same conclusions about the role of oxytocin on the HPA axis and the SAM axis. Therefore, it can be argued that strong evidence supports the role of oxytocin on the SAM axis and the HPA axis.

Finally, the limitation which has been discussed earlier is the use of the broad term ‘social support’. Based on findings it can be hypothesized that emotional support is beneficial for
health. Further research should examine the effect of the other kinds of social support.

From the 12 articles discussed in this thesis, it can be concluded that social support has a positive influence on health, by the suppressing/inhibiting effect of oxytocin on the SAM axis and HPA axis. In addition, the presence of high levels of oxytocin, may enhance directly the immune system, however, further research is necessary. Furthermore, future research can focus on the distinction of the different kinds of social support which may have differential effects on health outcome. Finally, the effects of oxytocin on health can be examined in people with a psychiatric disorder with a component of social impairment.
References


support enhancement intervention among married couples on ambulatory blood pressure, oxytocin, alpha amylase, and cortisol. *Psychosomatic Medicine, 70, 976-85.*


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