



## Intranasal oxytocin does not reduce age-related difficulties in social cognition

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### ABSTRACT

Oxytocin is a neuropeptide that plays a key role in social processing and there are several studies suggesting that intranasally administered oxytocin may enhance social cognitive abilities and visual attention in healthy and clinical groups. However, there are very few studies to date that have investigated the potential benefits of intranasal oxytocin (iOT) on older adults' social cognitive abilities. This is a surprising omission, because relative to their younger counterparts, older adults also exhibit a range of social cognitive difficulties and also show differences in the way they visually attend to social information. Therefore, we tested the effect of iOT (24 IU) versus a placebo spray on 59 older and 61 younger adults' social cognitive abilities and visual attention using a double-blind placebo-controlled within-groups design. While iOT provided no overall age-related benefit on social cognitive abilities, the key finding to emerge was that iOT improved ToM ability in both age-groups when the task had minimal contextual information, but not when the task had enriched contextual information. Interestingly, iOT had gender specific effects during a ToM task with minimal context. For males in both age-groups, iOT reduced gazing to the social aspects of the scenes (i.e., faces & bodies), and for females, iOT eliminated age differences in gaze patterns that were observed in the placebo condition. These effects on eye-gaze were not observed in a very similar ToM task that included more enriched contextual information. Overall, these findings highlight the interactive nature of iOT with task related factors (e.g., context), and are discussed in relation to the social salience hypothesis of oxytocin.

### 1. Introduction

Social cognitive function refers broadly to our ability to perceive, understand and react to the social cues sent out by other people. Although social cognitive abilities are essential for developing and maintaining social relationships, they are also associated with important non-social outcomes such as physical health, cognitive functioning and psychological wellbeing (Cornwell and Waite, 2009; Demir et al., 2012). As people enter late adulthood, protective factors such as strong social networks are particularly important (Cacioppo et al., 2010; Giles et al., 2005; Luanaigh and Lawlor, 2008), and therefore it is not surprising that a large literature has investigated how social cognitive function changes in late adulthood. Two key components of social cognitive function that have received considerable attention in the literature to date are: the ability to recognise facial emotions, also known as *emotion recognition*, and the ability understand mental states and intentions, often referred to as *theory of mind (ToM)*. Whereas

emotion recognition is regarded as a low-level perceptual process necessary to decode others' affective cues, ToM is regarded as a higher-level cognitive process necessary to interpret and reason about others' cognitive states (e.g., intentions, beliefs; Mitchell and Phillips, 2015). Emotion recognition and ToM are often referred to as distinct social cognitive components, however there is some evidence that they may share some common neuroanatomical components (Mitchell and Phillips, 2015). Relative to their younger counterparts (i.e., 18–30 years), older adults (i.e., 65 years+) have been consistently shown to experience difficulties in emotion recognition and ToM, and while these difficulties are related to broader age-related changes in cognitive function, these changes in cognitive ability do not fully account for the age differences seen in social cognition (for reviews of both of these literatures see, Henry et al., 2013; Ruffman et al., 2008). Given that age-related declines in social cognition are well established, the next important step is to establish whether there are any interventions that could potentially remediate these age-related difficulties.

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Age-related declines in neurotransmitters that regulate social behaviour (such as oxytocin and dopamine, [Ebner et al., 2013](#); [Ruffman et al., 2008](#)), have been identified as possible mechanisms for why older adults might experience difficulties on social cognitive measures. With this in mind, it seems reasonable to suggest that targeting neurotransmitters that are implicated in social processing might be a potential way to remediate age differences in social cognition.

Oxytocin is a neuropeptide plays a key role in regulating social behaviour. The potential benefit of intranasally administered oxytocin on social cognitive abilities has been of particular interest in the broader oxytocin literature. Research with younger adults has found that a single dose of intranasal oxytocin (iOT) enhances trusting behaviors ([Kosfeld et al., 2005](#); but see [Lane et al., 2015](#) who failed to find any effects of iOT on trusting behaviors), emotion recognition ability ([Lischke et al., 2012](#)), theory of mind processing ([Domes et al., 2007](#)), and sensitivity to eye gaze cues ([Guastella et al., 2008a](#)). Although such findings are encouraging, the benefits of iOT in clinical groups characterised by social impairments are even more promising, with studies showing improvements in key social cognitive skills in people with autism (for a review see [Preti et al., 2014](#)) and schizophrenia ([Guastella et al., 2015](#)). It should be noted that, although iOT has been found to produce a range of improvements in key social cognitive abilities, some studies have reported impairments in functioning after the administration of iOT. For instance, [Tabak et al. \(2016\)](#) found that iOT impaired *social* working memory but not *non-social* working memory in participants with high levels of social anxiety. [Jesso et al. \(2011\)](#) also reported impairments as a result of taking iOT whereby iOT had a differential effect on emotion recognition ability in participants with fronto-temporal dementia. Specifically, they found that iOT impaired the recognition of angry expressions but had no effect on the recognition of fearful, happy or sad expressions. These iOT-related impairments have also been reported in cognitive functioning more broadly, with younger males showing memory impairments after taking iOT compared to placebo ([Heinrichs et al., 2004](#); [Herzmann et al., 2012](#)). Therefore, although iOT has several promising effects, it is important to note that iOT can have negative effects under certain circumstances. Indeed, in their review of the social effects of oxytocin, [Bartz et al. \(2011\)](#) noted that over two thirds of studies which have examined the effect of iOT on social cognition have failed to find main effects of oxytocin. Instead, many of these studies report interactive effects with task type (e.g., task difficulty) or participant characteristics (e.g., anxiety levels), which suggests that the effectiveness of iOT is heavily influenced by contextual factors.

However, although iOT has been extensively studied in younger adults and clinical groups, only one study to date has examined the effect of iOT on social cognitive function in healthy older adults ([Campbell et al., 2014](#)). This is surprising, given that social cognitive difficulties are well established in older populations, and that iOT has been found to improve social cognitive functioning in clinical groups characterised by social deficits. Indeed, the specific need to better understand the role of oxytocin on social cognitive aging has been the focus of two prominent review articles ([Ebner et al., 2013](#); [Huffmeijer et al., 2013](#)).

[Campbell et al. \(2014\)](#) focused specifically on emotion recognition ability, and found that this social cognitive ability was enhanced for older but not younger males after taking iOT compared to placebo, and failed to find any effects in females. While this study was important in establishing the potential benefits of oxytocin in older age, it was limited by the use of exclusively static photographs of emotion. The key problem with using static stimuli is that they incorporate only one socio-emotional cue (i.e., facial expression), and this is not representative of how emotions are recognised in everyday social interactions, where non-verbal cues such as body language, voice tone, and gestures are also often relied on to decode both emotional and mental states. In addition, isolated expressions of emotion are perceptually very simple, and the key socio-emotional information that needs to be

attended to (i.e., facial expression) is relatively salient. Thus, if iOT is effective in increasing attention to the salient aspects of social stimuli (as will be discussed later), it is possible that these effects may be greater in more complex social situations where attention to more subtle details is required.

Another limitation of [Campbell et al.'s \(2014\)](#) study was the sole focus on emotion recognition ability, which is regarded as a relatively low-level affective social cognitive process ([Mitchell and Phillips, 2015](#)). Thus, it is not known whether higher level social cognitive processes such as ToM processing – which are critical for more complex social understanding – can also be enhanced with iOT. Therefore, important next steps in this literature are to assess the effects of iOT using social cognitive assessments that are more representative of every day social interactions, and to investigate whether the benefits of iOT extend to other core social cognitive functions known to decline with age, such as ToM processing.

Whereas most of the relevant literature now suggests that oxytocin has the potential to enhance social cognitive function, the mechanisms underlying these effects are not completely understood. The social salience hypothesis suggests that oxytocin modulates our attention to socially relevant cues in the environment, and this increased attention facilitates social cognitive processing ([Bartz et al., 2010](#); [Shamay-Tsoory and Abu-Akel, 2016](#)). Indeed, prior research with younger adults has found that iOT increases attention to the more socially rich areas of the face (i.e., the eye region, [Domes et al., 2013](#); [Guastella et al., 2008a](#)). Using a more ecologically valid paradigm, [Auyeung et al. \(2015\)](#) found that iOT enhanced gazing to the eye region of a face during real-time naturalistic social interactions. Together, these studies provide support for the theory that iOT modulates eye gaze to attend to the most socially important aspects of the visual field.

All of the studies to date that have examined the effect of iOT on visual attention have focused exclusively on younger adults. However, age-related visual biases to social information have been consistently identified, again pointing to the potential value of iOT in enhancing social cognitive function in late adulthood. For instance, older adults gaze less towards the eye region of a face compared to younger adults ([Circelli et al., 2013](#); [Grainger et al., 2017](#); [Murphy and Isaacowitz, 2010](#)), and also less towards the faces and more towards the bodies of people engaging in a discussion about a controversial topic ([Vicaria et al., 2015](#)). Because older adults attend less towards socially salient areas (i.e., eyes, faces), it has been suggested that they are not picking up on critical social information, and this could be negatively impacting on their social cognitive ability ([Wong et al., 2005](#)). Indeed, in the emotion recognition literature, some studies have established a relationship between the way older adults gaze at a face and their emotion recognition ability ([Sullivan et al., 2017](#); [Wong et al., 2005](#), but see [Circelli et al., 2013](#); [Grainger et al., 2017](#); [Murphy and Isaacowitz, 2010](#), who found no relationship). Therefore, it is of particular interest in this study to assess whether iOT can alter eye gaze patterns in older adults, and if any iOT-related changes in gaze patterns impact on social cognitive ability.

However, another important consideration in this literature is that although there have been several promising findings with iOT, concerns have been recently raised about the reliability of iOT studies ([Lane et al., 2016](#); [Walum et al., 2016](#)). Specifically, [Lane et al. \(2016\)](#) expressed concerns about a possible publication bias (i.e., the file drawer problem), and demonstrated that in their lab, the predicted effects of iOT were often non-existent. Although publication bias is not restricted to iOT research ([Maxwell et al., 2015](#)), it raises concerns that reported iOT effects in this literature may not be as robust as initially thought. Indeed, [Walum et al. \(2016\)](#) also expressed concerns about a potential publication bias in the iOT literature, along with several other methodological concerns. Perhaps the most critical concern they identified was the use of severely under-powered samples. In their review, [Walum et al.](#) reanalysed data from three iOT meta-analyses and concluded that the average iOT study with healthy adults had approximately 16%

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