Psychoneuroendocrinology 90 (2018) 148–156

Contents lists available at ScienceDirect

Psychoneuroendocrinology

journal homepage: www.elsevier.com/locate/psyneuen

To mirror or not to mirror upon mutual gaze, oxytocin can pave the way: A cross-over randomized placebo-controlled trial

Jellina Prinsen[a,*], Stephanie Brams[a,b], Kaat Alaerts[a]

[a] Research Group for Neuromotor Rehabilitation, Department of Rehabilitation Sciences, KU Leuven, Leuven, Belgium
[b] Movement Control & Neuroplasticity Research Group, Department of Kinesiology, KU Leuven, Leuven, Belgium

ARTICLE INFO

Keywords:
Oxytocin
Mirror system
Eye contact
Transcranial magnetic stimulation
Biological motion perception

ABSTRACT

The eyes constitute a highly salient cue to communicate social intent. Previous research showed that direct eye contact between two individuals can readily evoke an increased propensity to 'mirror' other peoples' actions. Considering the implicated role of the prosocial neuropeptide oxytocin (OXT) in enhancing the saliency of social cues and modulating approach/avoidance motivational tendencies, the current study adopted the non-invasive brain stimulation technique transcranial magnetic stimulation (TMS) to explore whether a single dose of intranasal OXT (24 IU) modulated (enhanced) a person's propensity to show heightened mirroring or motor resonance upon salient social cues, such as eye contact. The study involved a double-blind, placebo-controlled, cross-over trial with twenty-seven healthy adult men (19–32 y). By applying single-pulse TMS over the primary motor cortex during movement observation, it was shown that motor resonance was significantly higher when movement observation was accompanied by direct, compared to averted gaze, but that a single dose of OXT did not uniformly enhance this effect. Significant moderations of the treatment effect were noted however, indicating that participants with high self-reports of attachment avoidance displayed a stronger OXT-treatment effect (enhancement of motor resonance upon direct eye contact), compared to participants with low attachment avoidance. Particularly, while participants with high attachment avoidance initially displayed a reduced propensity to increase their motor resonance upon direct eye contact, a single dose of OXT was able to promote an otherwise avoidant individual's propensity to engage in motor resonance upon a salient social cue such as eye contact.

1. Introduction

Interpersonal interactions are extremely complex, involving both approach and avoidance behaviors toward other conspecifics. An important feature of successful social interaction and indicator of social approach is biobehavioral synchrony, or the coordination of biological and behavioral processes between interaction partners (Feldman, 2017). At the neural level, the brain's action observation system or mirror system is anticipated to play a key role in establishing interpersonal synchrony or 'resonance'. Several neuroimaging and neurophysiological studies show that distinct motor regions in fronto- and parietal cortices are increasingly activated not only when performing a particular action, but also when merely observing the same action performed by others, thereby providing a direct 'mirror-motor matching' or 'motor resonance' mechanism (Rizzolatti and Craighero, 2004). Overall, this 'mapping' of observed actions onto the observer's own motor system is suggested to form the basic mechanism by which others' actions, facial expressions or emotional states can be recognized, understood and acted upon (Cattaneo and Rizzolatti, 2009; Rizzolatti and Fabbri-Destro, 2008).

Albeit automatic, the propensity to 'synchronize' with conspecifics is anticipated to depend heavily upon the presented social context and prior social experiences of the individual (Wang et al., 2012). Among different social cues from the environment, mutual gaze forms a very powerful signal to express communicative intent and attention, and may therefore constitute a salient cue to evoke interpersonal synchrony or approach-related behavior (Grossman, 2017; Senju and Johnson, 2009). In line with this notion, studies from our and other labs showed that eye contact can rapidly and specifically facilitate automatic mirroring of others' actions, indicative of social approach (Prinsen et al., 2017; Wang et al., 2011a, 2011b). Here, we aim to explore the effect of social context (i.e. eye gaze) on motor resonance further and, in particular, whether administration of the prosocial neuropeptide oxytocin (OXT) can modulate this effect.

Endogenous OXT is synthesized in the hypothalamus where neurons of the paraventricular nuclei project to various cortical and subcortical

* Corresponding author at: Department of Rehabilitation Sciences, Tervuursevest 101, box 1501, 3001, Leuven, Belgium.
E-mail address: jellina.prinsen@kuleuven.be (J. Prinsen).

https://doi.org/10.1016/j.psyneuen.2018.02.016
Received 1 February 2018; Received in revised form 16 February 2018; Accepted 17 February 2018

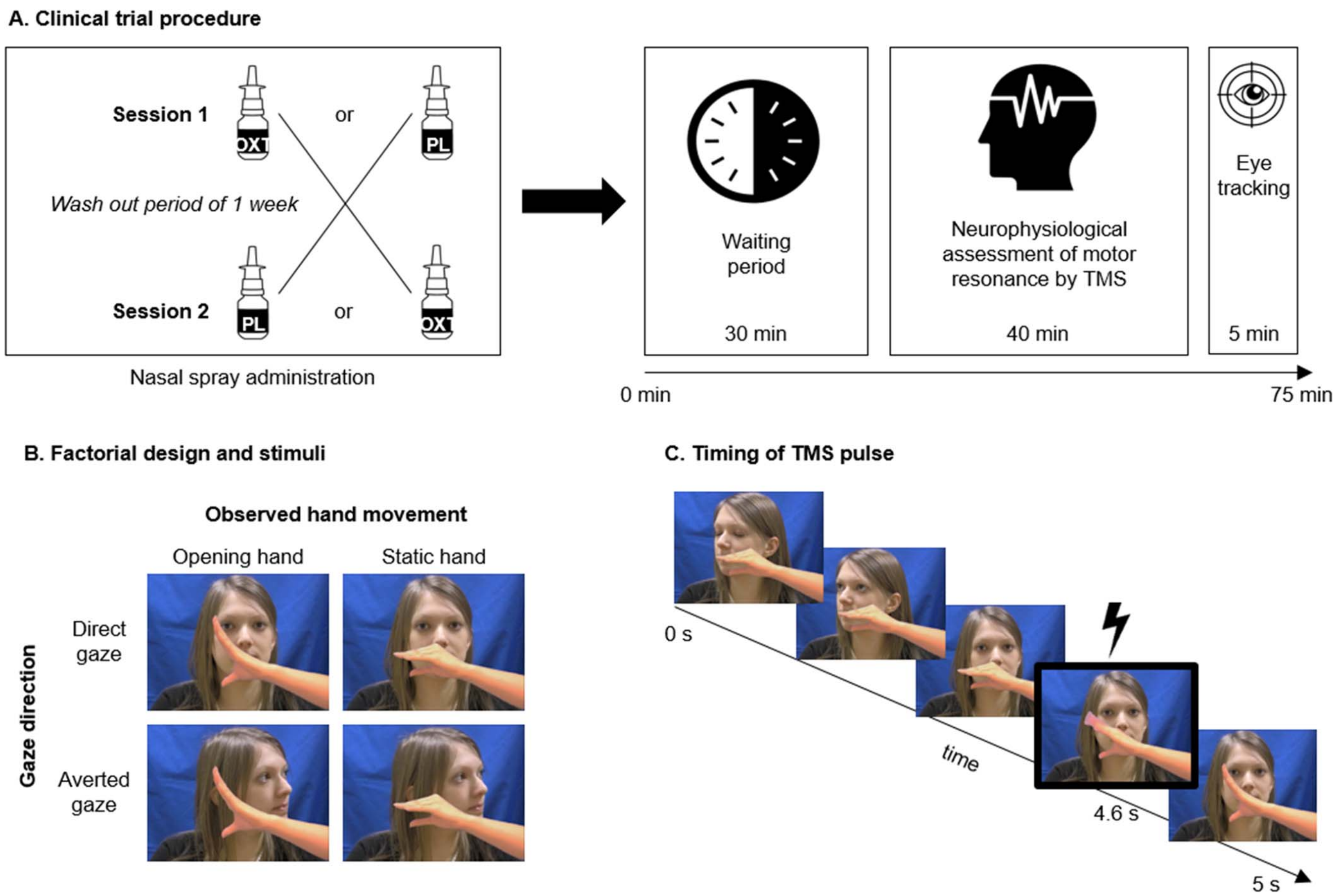

Fig. 1. A. Overview of the clinical trial procedure and timing schedule. B. Factorial design: video stimuli showing a model performing a simple intransitive hand movement (hand opening) or no movement (static hand), accompanied with either direct or averted gaze. The last still of each video clip is depicted. C. Example of the timing of the TMS pulse during the direct-open condition. Single-pulse TMS was delivered approximately 4.6 s after the start of each video clip, which corresponded to the execution phase of the observed hand opening movement.

brain areas involved in social behavior and socio-cognitive processes. Since the discovery that central OXT levels can be pharmacologically manipulated by means of intranasal administration of exogenous OXT (Born et al., 2002; Churchland and Winkielman, 2012), an ever-growing body of research has tested the implication of OXT on human sociality. Based on early findings reporting beneficial effects of OXT on social behavior, OXT has gained its prosocial reputation. However, this exclusively prosocial view of OXT has been nuanced by findings showing that the effects of OXT are strongly dependent upon the context in which the social interaction happens (Bos et al., 2012), as it can for example lead to a decrease in social cooperation towards members of an out-group (De Dreu et al., 2010).

Although not mutually exclusive, several mechanisms have been proposed by which OXT affects social behavior, namely (i) by enhancing the saliency of social cues; (ii) by modulating reward sensitivity and approach/avoidance motivational tendencies; and (iii) by reducing (social) anxiety (Bartz, 2016; Neumann and Slattery, 2015; Shamay-Tsoory and Abu-Akel, 2016). In particular interest for this study, eye-tracking studies showed that exogenously administered OXT promotes gaze towards the eye region of the communicator (Guastella et al., 2008) and increases eye contact during naturalistic social interactions (Auyeung et al., 2015). Increasing evidence also suggests that OXT can mediate the processing of the communicator's body language (Bernaerts et al., 2016; De Coster et al., 2014; Kéri and Benedek, 2009; Perry et al., 2010). For example, in terms of mapping of bodily cues, a handful of behavioral studies showed that a single dose of OXT reduced reaction times in an imitation task (De Coster et al., 2014) and enhanced biological motion perception or emotion recognition from so-called point-light display's (Bernaerts et al., 2016; Kéri and Benedek, 2009). An initial EEG study showed that OXT induced an increase in *mu*-rhythm suppression during biological motion perception, which is indicative of mirror-neuron activation (Perry et al., 2010).

With the present study, we adopted a novel paradigm to explore the prosocial effects of OXT-treatment on mirror-motor mapping or interpersonal motor resonance from a neurophysiological perspective. Particularly, by using the non-invasive and widely-used brain transcranial magnetic stimulation (TMS) technique, motor resonance upon movement observation was measured in order to obtain an unbiased neurophysiological measure of an individual's propensity to 'synchronize with' an observed model. In the past decade, single-pulse TMS has been used extensively as an assessment tool to measure resonant mirror activity in the observer's motor system during the observation of others' actions (see Fadiga et al., 2005 for a review). In particular, by applying a single magnetic pulse over the primary motor cortex, the underlying cortical neurons are activated, which elicits a motor evoked potential (MEP) from the corresponding contralateral muscles. Fadiga et al. (1995) showed that during the mere observation of others' actions, activity within the primary motor cortex becomes increasingly facilitated, as indicated by significant enhancements in MEP amplitudes elicited by TMS. By measuring the amplitude of the motor evoked potentials (MEPs) elicited by TMS under various experimental conditions, TMS can be used to monitor changes in putative mirror system activity in a relatively high temporal resolution.

As previous research showed that eye gaze provides a salient modulator of motor resonance (Prinsen et al., 2017; Wang et al., 2011a, 2011b), we expected to observe an enhancement of 'synchronization'