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A thorough review informed by transcriptomics of the neuroimaging genetics of oxytocin

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INTRODUCTION

Over the past few decades, a flurry of studies has shown that oxytocin (OT) plays a role in a number of the neurobiological determinants of human behavior and their impairment in mental illness. In particular, a neuroimaging genetics approach is assisting in elucidating the effects of OT pathway gene variations on the human brain. All previous findings from human neuroimaging (epi) genetic studies of OT-related genes are presented and discussed in detail for the first time in this review. Utilizing data from the Genotype-Tissue Expression project, we investigated the potential functional effects of genetic variations on the human transcriptome to enhance our mechanistic interpretation of these findings. Consequently, we highlight several (epi) genetic factors that modulate brain responses to intranasal OT, map brain pathways linking OT genes to disease, and provide an up-to-date summary of brain circuits found to be impacted by OT-relevant (epi) genetic variability. Last but not least, we make a few suggestions that we think could help future research in the field [1].

DESCRIPTION

Oxytocin (OT) is a hypothalamic nonapeptide that has a prominent role in the development and regulation of human socio-affective behavior, as we and others have reviewed. Oxytocin (OT) has long been recognized for its hormonal function during labor and lactation. The regulation of food metabolism, neuroinflammation, and pain are additional functions of OT. This increased significance of occupational therapy, specifically in brain function, sparked interest in its modulation as a promising new therapeutic approach for a number of brain disorders that lack effective treatments (such as Prader-Willi syndrome, autism spectrum disorder, schizophrenia, migraine, obesity, and others). However, we believe that mechanistic pathophysiological issues need to be resolved before the psychotherapeutic potential of occupational therapy can be fully realized [2].

Understanding the OT system is made easier by the advancements in human genome mapping and the realization that intranasal administration of OT is effective. Using functional magnetic resonance imaging (fMRI), electroencephalography (EEG), or positron emission tomography (PET), we can assess how variability in human behavior and cognition, as well as their neurocorrelates, may be a function of acute variation in OTergic tonus caused by pharmacological potentiation of intranasal

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OT administration and chronic variation in OTergic tonus caused by naturalistic genetic diversity These two approaches-pharmaco-neuroimaging and neuroimaging genetics-have been at the center of human OT research alongside measurements of OT in biological fluids [3].

The neuroimaging (epi) genetics studies reviewed here investigate whether or how a particular genetic polymorphism or gene's methylation status influences functional (task-related, resting-state, neurochemical, or structural) brain neuroimaging phenotypes. By assessing the impact of naturalistic variation between individuals, in a substance's level and signalling degree that is within normal physiological range and free from artificial manipulation, this method complements pharmacological neuroimaging, which typically uses a randomized control trial design. In neuroimaging pharmaco-(epi) genetics designs, both of these approaches can, of course, be combined to explain how the brain's response to a particular pharmacological manipulation (like intranasal OT) may depend on genetic variations or epigenetic nuances (especially those that are directly part of the OT pathway). However, the lack of knowledge regarding the functional consequences of the studied polymorphisms, particularly those that are located in non-coding regions or do not result in amino acid changes, severely limits the interpretation of the majority of the findings [4].

Neuroimaging (epi) genetics studies of the OT system have grown significantly over the past five years, despite the fact that the vast majority of evidence implicating OT in human physiology has arisen from its pharmacological administration (reviewed elsewhere). We aim to provide a systematic, in-depth, and integrated overview of these findings in order to better understand and make such research more useful, given the numerous genetic variations, neuroimaging modalities, brain regions, and clinical populations investigated. In order to answer the primary question, we present the first comprehensive overview of all OT neuroimaging (epi)genetics advancements to date in this review. What effects does the OT system's inter-subject genetic variability have on brain structure and function? as well as the secondary inquiry, "How are the latter effects altered in psychiatric pathologies?" A previous systematic review has been published, specifically for the OT's receptor genotype effects on functional connectivity in the resting state. We include all of the single nucleotide polymorphism (SNP) and methylation findings that have been reported so far for the three genes that code for the OT/neurophysin I prepropetide (OXT), the receptor for OT (OXTR), and the cluster of differentiation 38 glycoprotein (CD38) genes. These three genes are the main players in the OT pathway. In order to better map the pathophysiological pathways of OT genes in the brain, we include studies utilizing any neuroimaging method, including MRI, EEG, magnet encephalography (MEG), PET, and single-photon emission computed tomography (SPECT), as well as healthy individuals and clinical samples. In conclusion, we also include all intranasal occupational therapy (OT) pharmaco-neuroimaging (epi) genetics studies in order to summarize all nuances of (epi) genetics that may influence a response and, consequently, aid in its prediction. The reviewed findings are discussed, reconciled with existing theories regarding the role of occupational therapy in human behavior and physiology, and their potential limitations are laid out. We determine the effect of each genetic variation on brain gene expression in order to facilitate a more mechanistic discussion of these studies. We use a publicly accessible genetics-transcriptomics database for this purpose: The project known as Genotype-Tissue Expression (GTEx). Using this tool, we've compiled a comprehensive list of functional variations that we think will be useful for advancing research in the future.

We hope that our evaluation helps: Aid in the design of enhanced neuroimaging (epi) genetics studies, broadening our understanding of occupational therapy's role in human neurophysiology, health, and disease; and, consequently, guide the rational development of novel Steric neuropharmacological treatments; and encourage the creation of intranasal occupational therapy pharmacogenetics biomarkers so that we can determine who is most likely to benefit from such treatments [5].

CONCLUSION

To find relevant studies that could be included in the current review, we followed the PRISMA guidelines for systematic reviews. Starting with the 119 studies that were initially identified and working our way down to the 62 included in the flowchart. Using the query, "all existing neuroimaging (epi) genetics studies of the OT system-related genes in humans," we searched Medline to locate all oxytocin, as well as (gene, genotype, polymorphism, genetic marker, methylation, or epigenetic) and (MRI, EEG, MEG, PET, or SPECT) additionally, all references in the retrieved articles were manually checked for any missing articles. Utilizing the smart group function of ENDNOTE, duplicate studies were eliminated.

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CONFLICT OF INTEREST

None.

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