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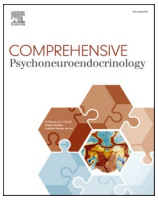

A journey from speech to dance through the field of oxytocin

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ABSTRACT

In this article, I am going through my scientific and personal journey using my work on oxytocin as a compass. I recount how my scientific questions were shaped over the years, and how I studied them through the lens of different fields ranging from linguistics and neuroscience to comparative and population genomics in a wide range of vertebrate species. I explain how my evolutionary findings and proposal for a universal gene nomenclature in the oxytocin-vasotocin ligand and receptor families have impacted relevant fields, and how my studies in the oxytocin and vasotocin system in songbirds, humans and non-human primates have led me to now be testing intranasal oxytocin as a candidate treatment for speech deficits. I also discuss my projects on the neurobiology of dance and where oxytocin fits in the picture of studying speech and dance in parallel. Lastly, I briefly communicate the challenges I have been facing as a woman and an international scholar in science and academia, and my personal ways to overcome them.

1. An unusual start: from linguistics to neuroscience

Since I can remember myself, from early to middle and high school, I have always been fascinated by what we call "language", a word that took many different meanings throughout my life. I remember myself listening carefully to what my family and friends had to say, and more importantly to how they were saying it; I was equally careful with the words I was picking to express a thought or a feeling. As I am seeking to understand the origins for this early inclination of mine, I recall my grandparents, teachers and ardent literature readers, who would recite poetry to me and ask me questions on the etymology of the words I was using. This passion for language also stems from my parents' polyglossia, which they instilled in me: I currently speak 6 languages (Greek, English, Spanish, Italian, French, Catalan), including being a proficient reader of texts written in Ancient Greek and Latin.

I soon started to write my own prose and poetry and won my first important literature award at the age of 7 (Kid Fairytale Prize from Minoas Publications), followed by an award in poetry at the age of 22 (Panhellenic Poetry Competition). Although I was fond of reading and writing, I was also an excellent student at all the other school subjects, including in Mathematics, Physics, and Biology, and was selected to represent my school in the most competitive national competitions in Mathematics (e.g., "Thales" competition). In fact, in almost all years of middle and high school I was ending the school year with a clean 20/20 grade. This meant that it was not the grades themselves that guided my future academic choices, but my own deep wishes and passions.

In an academic world, in Greece and worldwide, where the "humanities vs. sciences" distinction reigned, I had to take a decision as to which studies would enable me to best delve into the wonders of the vehicle we use for communication that I so much cherished: language. I decided to go for the School of Philosophy in Athens (National and Kapodistrian University of Athens), and to choose the specialization path of Philology and Linguistics. At that point, the field of Linguistics was at, what I came to later understand, a crucial nexus: one the one hand, there were the theoretical linguists, who thought that to dissect the mechanisms of language, one had to study language itself; on the other hand, either neuroscientists or linguists turning to neuroscience had begun to postulate that one cannot understand what language is, unless through looking into the brain. The University of Athens was almost exclusively driven by theoretical linguists, who exposed us to the great lessons of Noam Chomsky, among others, and who left me fully convinced that I had picked the right path that would lead me to understand the inner workings of language.

It was not until I saw an advertisement on the University's walls about applying for an Erasmus scholarship that enables undergraduate students to study for a semester at a different European University, including in Spain. This is where another important pillar of my life comes in to explain my feverous willingness to take up this opportunity:

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flamenco. I had been dancing flamenco since I was little, and, truly, flamenco was one of those elements in life that made (and still makes) all the rest come together. Sometimes, I realize that my stellar grades in school were because of flamenco; I had created a personal motivation system, where I was telling myself I would not go to my dance classes unless I had finished my homework. Looking forward to a flamenco class had always propelled me to finish my homework in a concentrated and effective manner. And here was in front of me my chance to marry both my passions for Linguistics and flamenco by traveling to the mecca of flamenco in the world: Seville.

What I did not know was that, back at that time, the University of Seville, was abounded by professors who were studying and teaching what is called "Neurolinguistics", the field that had come up to bring closer together the fields of Neuroscience and Linguistics. I was astounded to learn which brain regions light up while we are speaking and about the brain plasticity during language learning in the first years of our lives. In very little time, I came to realize that unless I worked on the brain circuitry of language, I would never be able to shed light on how language came about and why humans speak the way they speak. And this is how flamenco led me to choose an academic destination that would change my scientific understanding of language, and how art initially played a role in a cascade of decisions that ended up making me a Master's holder of the "Cognitive Science and Language" program of the University of Barcelona. In two years' time, I passed from studying the "form" of language for my undergraduate thesis [1] to deciphering the brain white matter patterns that underlie language learning [2], and the lateralization differences in the brain regions involved in language in men vs. women, via Magnetic Resonance Imaging [3].

2. From humans to songbirds: from oxytocin to mesotocin

As a Doctoral graduate student, under the supervision of Cedric Boeckx at the University of Barcelona and of Erich Jarvis at Duke University and during his transition to Rockefeller University, I came to form the hypothesis that oxytocin could be playing an important role in language production and learning in humans [4]. Oxytocin (*OT*) acts as a hormone, neuromodulator or neurotransmitter that functions mainly through the oxytocin receptor (*OTR*) to regulate a diverse set of

Table 1
Main biological functions of *OT* in vertebrates. First column: old nomenclature for *OT* in different lineages. Second column: revised universal vertebrate nomenclature proposed in Refs. [8,9]. Third column: major biological functions of *OT* in each lineage. Color shading: terms that fall under the same general biological function (e.g., purple for 'sexual behavior' processes: courtship, pair-bonding, grooming, sperm ejaculation, reproductive behavior, sexual behavior etc.; light green for 'mothering' processes: female pregnancy, uterine contractions, egg-laying, nesting etc.). Partial reproduction with permission from the Supplementary Table 1 in Refs. [8,9].

Old nomenclature	Universal Vertebrate Revision	Functions
Oxytocin, Neurophysin, Mesotocin, Isotocin, Glumitocin, Valitocin, Aspargtocin	Oxytocin (*OT*)	**Mammals:** drinking (Verty et al. 2004), eating (Verty et al. 2004), female pregnancy (Arthur et al. 2008), grooming (Marroni et al. 2007), heart development (Jankowski et al. 2004), lactation (Leng et al. 2008), mating (Insel and Hulihan 1995; Witt and Insel 1994), aggression (Bosch et al. 2005), memory (Larrazolo-López et al. 2008), blood pressure regulation (Petersson et al. 1996), ossification (Elabd et al. 2007), uterine contractions (Magalhaes et al. 2009), digestive system regulation (Wu et al. 2003), pain perception (Yang et al. 2007), estradiol response (Jirikowski et al. 1988), sleep (Putnam et al. 2008), social behavior (Lukas et al. 2011), sperm ejaculation (Filippi et al. 2003), sensory perception (Marlin et al. 2015) **Birds:** pair bonding (Klatt and Goodson 2013), social behavior (Goodson et al. 2004), locomotion (Jonaidi et al. 2003), food intake (Jonaidi et al. 2003), aggression(Goodson et al. 2015) **Reptiles:** nesting behavior (Carr et al. 2008), egg-laying (Carr et al. 2008) **Amphibians:** reproductive behavior (Jean-Luc et al. 2006) **Coelacanths: -** **Fish:** social vocalizations (Goodson and Bass 2000; Goodson et al. 2003), social behavior (Zimmermann et al. 2016), nocifensive behavior (Wee et al. 2019) **Sharks:** probably osmoregulation (based on gene expression in kidney, rectal gland and intestine) (Gwee et al. 2009) **Lampreys/Hagfishes: -**

biological processes, some of which include uterine contractions, milk ejection, bond formation, copulation and orgasm, stress suppression, thermoregulation, olfactory processing, auditory processing, and eye contact [5–7] (Table 1).

This possible role of oxytocin in language was not part of any of my supervisors' research agenda; it was my own hypothesis that I brought to the table during the first month of my graduate studies. This is how I came up with it: in the summer after finishing my Master's studies, I delved into scientific articles, books and documentaries that would prepare me for a PhD in neuroscience, a field in which I still had lots to learn. My synthesis of the information I had chosen for my summer education led me to the hypothesis that an important, possibly necessary, aspect of language learning in human babies is the socially rewarding feedback they receive from their parents or caregivers during their speech attempts in the first years of their lives [40]. Back then, there was only some suggestive evidence. For example [41], exposed infants, reared in an English-speaking environment, to Mandarin Chinese, by exposing them to a) only audio recordings of Mandarin Chinese; b) audiovisual stimuli (i.e., videos) where people were speaking in Mandarin Chinese; or c) live-interactive learning with a Mandarin Chinese speaker. They found that only the latter (c) gave rise to successful language learning. Nonetheless, this experiment was made for second-language learning, leaving unanswered the question of whether the primary speech learning mechanisms rely on motivational and rewarding mechanisms provided by social interactions.

And this is where *OT* comes into play. My literature exploration of the social reward and motivation brain pathways led me to oxytocin, but there was no one, to my knowledge, that had suggested back then a role of oxytocin in the brain pathways of human language. I was only able to find relevant evidence in the auditory and vocal behaviors of non-human animals. For example, *OT* and *OTR* knock-out infant mice were found to emit fewer ultrasonic vocalizations when compared to wild-type mice [42,43], while *OTR*-containing neurons in the mouse auditory cortex were identified to both be involved in auditory processing of pups' ultrasonic vocalizations [28] and to be left-lateralized [44]. These studies, along with other evidence at different levels of analysis (e.g., interaction of *OT* with key genes in gene pathways with an established role in language, such as the *FOXP2-CNTNAP2* pathway [4]) became the backbone of my proposal to study the implications of *OT* in human language.

Although up to that point I had only worked with human subjects, I took up on the suggestion of Dr. Jarvis to first test this hypothesis in songbirds. Birdsong in his and others' laboratories was being used as a model to understand human language, and, in particular, "vocal learning", a core component of language. Vocal learning is the ability to imitate complex sounds and is found to date in only a few independently evolved species of mammals (humans, bats, cetaceans, sea lions and elephants) and birds (songbirds, parrots and hummingbirds) [45,46]. Testing the social reward mechanisms of birdsong in zebra finches, a songbird species that is widely used in research, meant that I would need to immerse myself into experiments I had never run before. Thanks to a lot of self-learning, generous help of other lab members, and guidance from my mentors and collaborators, I managed to enter into the beautiful world of songbirds.

I ran my first behavioral experiments at Duke University, followed by research at Rockefeller University, where Dr. Jarvis transitioned, and Hunter College (City University of New York), the latter in the context of our collaboration with Dr. Ofer Tchernichovski, who instilled in me his unique curiosity for the finches' vocal learning behavior. One of my first most exciting findings was on the role of social reward in vocal learning in zebra finches, where I showed that, when exposed to two different types of songs in isolation vs. a socially rewarding context, male finches end up learning the song of the socially rewarding context [47]. This was the first direct piece of evidence for my initial hypothesis [48] that social reward gates vocal learning.

Up next, my plan was to test the hypothesis [48] that, in songbirds, *OT* subserves these social reward mechanisms of vocal learning. This is where an obstacle came up: I was not able to find in the zebra finch genome (version Taeniopygia_guttata-3.2.4) any gene that was called "oxytocin" or, even, "oxytocin receptor". Searches in the zebra finch genome, and other avian genomes, based on mammalian *OT* and *OTR* gene sequences were leading me to genes that were named as "mesotocin", for the ligand, and "mesotocin receptor" or "vasotocin receptor 3" for the receptor (Table 2). The literature back then was equally perplexing, containing an array of different names [29,30,49].

I decided to reach out to several scientists working on the endocrine system of avian species, and their responses on the matter were even more bewildering. These were the most prominent explanations: a) the avian mesotocin just shares a high sequence identity with the mammalian oxytocin, but in reality they are two different genes, and birds do not have oxytocin; b) the avian mesotocin and the mammalian oxytocin are the same genes, but we are using different names because their function/gene expression/gene sequence is different [50]. If a) were the case, then this would mean that oxytocin either had not evolved in the avian lineage or that it had been deleted, and that, either way, I would not be able to study the oxytocin system in songbirds; if b) were the case, then this would mean that scientists base gene nomenclature on parameters, such as gene function or sequence, that are known to be variable across species. If the latter practice were adopted across all genes, then we would be using a nomenclature that oftentimes should not truly reflect evolutionary relationships, but relationships between specific metrics: e.g., mouse and human gene sequences of the "oxytocin receptor" share a high sequence similarity, hence they are given the same name, but human and zebra finch sequences for the same (evolutionary orthologous) gene do not, hence the sequence of the former is called "oxytocin receptor" and of the latter "vasotocin receptor 3". This lack of clarity in the field urged me to resolve first the issue of whether songbirds, and avian species in general, have or do not have the gene that in mammals is called "oxytocin".

Proposing a universal nomenclature for the oxytocin-vasotocin ligand and receptor families.

To tackle this issue, I needed to get a good handle on comparative genomics and phylogenetics, and on tools and methodologies that I had little experience in. This required, once more, a lot of self-learning, paired with the valuable help I was thankful to receive from my labmates and mentors. Progressively and during my transition as a Post Doc at Rockefeller University, I was able to advance genomic methods that enabled me to find out whether and which oxytocin-vasotocin (*OT-VT*) ligands and receptors are present in 35 vertebrate and 4 invertebrate species' genomes. The reason why we included so many species in our analysis was because, although the initial conundrum was for the relevant genes in avian species, we soon realized that the rest of the vertebrate species were also suffering from an inconsistent nomenclature (Table 2).

My modus operandi was to compare across species not only the sequences of the genes of interest (through pairwise comparisons and phylogenetics), but importantly to compare the genes surrounding these putative genes of interest (synteny analyses). What I found after hundreds of pairwise sequence identity comparisons was that often clearly orthologous genes (e.g., gene X in rat and mouse) have a higher sequence identity with another paralogous gene (e.g., gene X in mouse with gene Y in rat) and not their orthologous one, and that sequence identity is not a stable parameter on which we can base our gene orthology identification and gene nomenclature. Unlike the instability of gene sequences across species, I found that the gene territory (or, the synteny), namely the genes that surround gene X in one species and the same orthologous gene X in another is widely conserved. Using a combination of different synteny analyses (i.e., in a 10-gene window, 100-gene window, and chromosomal windows), I managed to clarify gene orthologous and paralogous relationships across vertebrate species, which led to a proposal of a universal vertebrate gene nomenclature for these gene families. Considering that sequence identity comparisons (e.

Table 2
Previous and proposed terminology for genes encoding *OT* and *VT* ligands and receptors in vertebrates. Long (for example, *VTR1A*) and short (for example, *V1A*) versions of the gene symbols are given. Aliases include terminology in the NCBI gene database. (Reproduced from Table 1 of [8,9] with permission).

Mammals	Birds	Turtles and crocodiles	Frogs	Fish	Sharks	Universal vertebrate revision
Oxytocin (*OXT*, *OT*, *Oxy*) Neurophysin (*NPI*) Mesotocin (*MT*)	Mesotocin (*MT*, *MST*) Oxt-like Neurophysin-1-like	Mesotocin (*MT*, *MST*)	Mesotocin (*MT*, *MST*)	Mesotocin (*MT*) Isotocin (*IT*, *IST*) Glumitocin Neurophysin *IT-1*-like, *IT-NP*	Valitocin Aspargtocin	Oxytocin (*OT*)
Arginine vasopressin (*AVP*, *ARVP*, *AVRP*, *Vp*, *Vsp*) Neurophysin II (*NP2*) Lysine vasopressin Phenypresin	Vasotocin (*VT*)	Vasotocin (*VT*)	Vasotocin (*VT*)	Vasotocin (*VT*) *VT-NP*, *avpl*, *vsnp*	Vasotocin (*VT*)	Vasotocin (*VT*)
OXTR, *OTR*	*VT3*, *MTR*	*OXTR*	*MesoR*, *OXTR*	*ITR*, *OXTR*, *itnpr*-like 2, *itr2*	*OXTR*	Oxytocin receptor (*OTR*)
AVPR1a, *V1aR*, *V1A*	*VT4*, *VT4R*		*Avpr1*, *VasR*	*Avpr1aa*, *VasR*, *Avpr1ab*		Vasotocin receptor 1 A (*VTR1A*, *V1A*)
AVPR1b, *V1bR*, *(A)VPR3*, *V3*, *VIBR*	*VT2*, *AVT2R*					Vasotocin receptor 1B (*VTR1B*, *V1B*)
	VT1, *AVPR2*		*Avpr2*.2	*V2C*, *V2bR2*, *Avpr2.2*, *V2L* *V2B*, *V2BR1*, *V2R,OTRI*, *nft*, *avpr2*	*V2C*, *V2bR2*	Vasotocin receptor 2 A (*VTR2A*, *V2A*) Vasotocin receptor 2B (*VTR2B*, *V2B*)
AVPR2, *V2R*, *VPV2R*				*Avpr2bb*, *V2A*(*2*), *avpr2a* (*a*)		Vasotocin receptor 2C (*VTR2C*, *V2C*)

g., with BLAST alignments [51]) have been used as the canon to reveal orthologous and paralogous relationships so far, with this study I shifted the focus of what defines gene orthology from what lies "inside" the gene (sequence) to "outside" of it (synteny).

I believe this study is a great example that you can never expect where science will take you. Sometimes, to address a question, in this case, if *OT* is involved in vocal learning in songbirds, one needs to resolve other pending questions that are on the way, in this case, whether songbirds have *OT* to begin with. Although the resulting findings far exceeded the scope of this question, this study was necessary for scientists like me to be confident on the exact system they are working on and provided the needed evidence for my project that birds, including songbirds, have the same orthologous *OT* and *OTR* genes that are found in the rest of the vertebrates.

3. Impact of the unified gene nomenclature to the research community

In the short time it has been published, our methodology and proposal for a universal vertebrate gene nomenclature for the *OT-VT* ligand and receptor families has been adopted in a variety of studies across vertebrate lineages [52–55] and it has influenced the NCBI and ENSEMBL annotation groups in using synteny as the primary evidence when it comes to annotate newly sequenced genomes, such as those that I contributed to in the context of the Vertebrate Genomes Project [56]. Further, our methods for synteny analyses have worked as the foundation of a subsequent project I co-coordinated on the evolution of the *OT* pathway genes in both vertebrates and invertebrates [57].

Our findings have also had an impact beyond the fields of neuroscience and genomics; for example, they were used by structural biologists to explore the mechanisms responsible for the cellular physiology of G protein coupled receptors [58]. Our identification of the orthologous and paralogous gene relationships (or, of "which gene is which") across vertebrates provided their research with the correct genes to work on, whose study led them to identify that cation coordination is required for both *OT* binding and *OTR* activation.

In the context of the aim of this Special Issue to debunk the myth that *OT* is just a female hormone, I could say that with this work, at the very least, we debunked the myth that *OT* is just a mammalian hormone. Now we can support with evidence that *OT* is the same orthologous gene in all vertebrate lineages (e.g., mammals, birds, amphibians, fish, cyclostomes), not an "analogous" gene or an "oxytocin-like" gene, going by different names in different species and lineages (e.g., mesotocin, isotocin, glumitocin, valitocin, and neurophysin) (Table 2). I find that debunking the "female hormone" myth goes hand-in-hand with debunking the "mammalian hormone" myth, since essentially the functions in females with which *OT* has been traditionally linked are also mammalian-specific (e.g., birth uterine contractions and lactation). Upon reviewing the so far identified functions (Table 1) of *OT* across vertebrates, it becomes tangible that *OT* is far from being involved in only these mechanisms.

Our proposed unified gene nomenclature also met some pushback. For example, some authors cite our paper in their work to support gene orthology between the mammalian *OT* and the orthologous gene they study in other vertebrates (e.g., in teleost fish [59], and waxbill [60]) but do not adopt in their manuscript our proposed nomenclature, or use it interchangeably with the old nomenclature [58]. According to some of these authors' experience that they communicated to us (e.g. Ref. [58], their use of the traditional symbols was due to following reviewers' suggestions to stick to the traditional nomenclature. In my experience as well, although in 4/5 scientific studies I have published on the *OT-VT* system since then [50,61], both editors and reviewers welcomed the use of our unified gene nomenclature, in one case [62], one of the editors would not allow the use of the new nomenclature, with arguments ranging from gene nomenclature needing to echo gene identity to nomenclatural changes happening over 100 years and not with a single paper. Nonetheless, we were permitted to include in the conclusions of the paper [62] the scientific reasons that made us propose a universal nomenclature.

The most organized reaction to our proposal came from Ref. [63] who argued that only minor nomenclatural changes are needed in this gene family, and that changes in nomenclature should be based on tradition, name stability, phylogeny, identity and gene function. One of their main arguments was that a standardized system of nomenclature already exists, "first established in vertebrates 30 years ago", although we provided challenges for their practices with scientific evidence. In our response [50], we provided further phylogenetic evidence for our gene orthologies, based on analysis using high-quality genomes, and proposed evidence-based criteria for gene nomenclature decisions beyond the *OT-VT* ligand and receptor families, in the following order of reliability: synteny, phylogenetic inference, sequence identity and gene function. We also proposed the creation of a Universal Gene

Nomenclature Committee that will involve scientists working on sequencing, assembly, annotation, phylogeny and genome evolution, as well as on the respective lineages and genes for all life. I believe such committee will enable all scientists to speak the same language for the first time in history, a language that will be evidence and evolution-based, something that will revolutionize translation of findings across species and clinical research.

4. Using the evolution of the oxytocin-vasotocin receptors as a lens to understand vertebrate genome evolution

One of the most interesting -and unexpected-ramifications of the 2021 study was that our comparative genomic findings led us to put forward a scenario for the evolutionary history of the oxytocin-vasotocin receptors (*OTR-VTR*) and, by extension, for vertebrate genome evolution in general, that is different from the traditionally accepted one. According to the most influential hypothesis for vertebrate genome evolution, first proposed by Ohno [64] 50 years ago, vertebrate genomes evolved through two (or possibly three) rounds of whole genome duplication: the first in the origin of cephalochordates (e.g., amphioxus) and vertebrates and additional ones within vertebrates. This hypothesis was later reinforced with the finding of four *HOX* gene clusters in mammals [65], construed as the possible results of two rounds of whole genome duplication (2 R of WGD). Most studies since then, using phylogenetic analyses only [66–68], or a combination of synteny and phylogenetic analyses [69,70], have interpreted their findings considering the 2 R hypothesis as the only evolutionary scenario *a priori*.

In both the original 2021 study and a follow-up study I single-authored to further delve into this topic, I performed analyses of the chromosomes or scaffolds containing *OTR-VTR* across different vertebrate species and mapped these segments back to reconstructed karyotypes of putative vertebrate or chordate ancestors. This kind of analysis, that I named "ancestral analyses" in these studies, allow to identify the location of genes, in this case the *OTR-VTR* genes, in the putative chromosomes of the ancestor of all vertebrates or chordates. Tracing the evolutionary history of a gene family back to the stem of vertebrates uniquely sheds light to the rounds of WGD this family possibly underwent. As I explained above, the evolutionary scenario I was expecting to find was that written in the textbooks, namely that the *OTR-VTR* underwent 2 R of WGD.

Contrary to this expectation, my findings pointed to two possible scenarios, the one being consistent with the traditionally accepted 2 R of WGD, with the first occurring in the gnathostome-lamprey ancestor and the second in the jawed vertebrate ancestor, but the other pointing to only 1 R of WGD in the common ancestor of lampreys and gnathostomes, followed by segmental duplications in both lineages. Combining the data from the ancestral, synteny and phylogenetic analyses, I put forward that the scenario consistent with 1 R of WGD is more parsimonious. Although the analysis of one gene family is not able to capture the full complexity of vertebrate genome evolution, this alternative scenario may pave the way for vertebrate genome evolution to be seen through a prism that is different to the one used in the past 50 years.

5. Oxytocin in vocal learning avian species

With the gene orthologies clarified, I was finally able to work on the *OT* system in songbirds, without ambiguities as to which system I was working on and whether my findings would be translatable to humans or not. One of the first experiments I tried included an intranasal administration of an *OT* antagonist in adult male zebra finches to assess whether it would have any impact on the song they sing to females to attract them.

Male zebra finches sing two types of song, the one being the "undirected" song, which is the type of song they sing by themselves, possibly to practice, and another, being the "directed song", which they sing to females [71]. These two types of song have some established differences between them [71], including in the number of introductory notes the finches sing before they start singing the main motif of the song, which are significantly more during directed singing, possibly to attract the attention of the female. In my experiments, I found that the *OT*-antagonist treated males had a significant drop in the number of introductory notes in their directed song, which made their "love song" more similar to the undirected song they sing without a female [47]. This points to *OT* being necessary for an important feature (i.e., introductory notes) of directed zebra finch singing, which, as far as we know, serves the purpose of attracting the female finches to copulate [71].

The zebra finch was not the only avian species I worked on. A presentation I gave at a conference attracted the attention of Dr. Kazuo Okanoya (University of Tokyo and RIKEN Brain Science Institute), an expert in the songbird field, to pursue understanding together the role of *OT* in the singing and general behavioral differences identified in two very closely related songbird species/strains: the white-rumped munias and the Bengalese finches. These two species have a very interesting story: more than 250 years ago, the white-rumped munias were imported and brought into captivity from China to Japan [72]. They were initially used to foster exotic birds, and were artificially selected against aggression, which gave rise to a domesticated "version" of these species, called Bengalese finches [73]. These domesticated Bengalese finches are not only less aggressive and fearful; they also show different pigmentation in their plumage and, importantly, sing a more complex song than the white-rumped munias [74]. This has led scientists to hypothesize that the higher vocal learning complexity in Bengalese finches might have occurred as a by-product of their domestication. Since *OT* has been highlighted in research focused on differences between domesticated and wild species [75], and since my findings in zebra finches suggested a role of *OT* vocal learning, we hypothesized that it made a great candidate for studying the neurobiology underlying these species' behavioral differences.

In a study I co-led with Dr. Yasuko Tobari we compared the *OT* nucleotide sequence and synthesis between the wild white-rumped munias and the domesticated Bengalese finches [75]. We found specific nucleotide changes in the regulatory regions of *OT*, both within the Bengalese finch population, and in comparison to the white-rumped munias. Some of these changes we identified fall in transcription factor binding sites and are well conserved in vertebrates in general, or in the avian lineage in particular, something that suggests they might be sites that are responsible for functional effect differences in these species. Additionally, we showed, via real-time quantitative PCR, a significantly lower *OT* mRNA expression in the diencephalon of the Bengalese finches relative to munias, implying there is less hypothalamic *OT* synthesis in the domesticated strain, although, puzzlingly, the expression was significantly higher in the Bengalese finch cerebrum compared to munias. Our brain region-specific gene expression results did not match those reported in other domesticated species (e.g., rats and mice) [76], where more *OT* production was found for the domesticated strain. Our interpretation was that these differences from other domesticated species might be due to different domestication pathways (laboratory vs. pet domestication), and/or to different domestication processes in the mammalian vs. the avian lineages.

Regardless of the specific interpretation, our findings on differences on the *OT* gene sequence and brain expression in two very closely related species that differ in their vocal learning complexity indicates that *OT* could subserve these differences. Studies that were run before [49,77] or after ours [54,78] in zebra finches pointing to: a) the *OTR* being differentially expressed in their vocal learning nuclei [49,78]; b) an age-dependent downregulation of *OT* in the hypothalamic paraventricular nucleus during the first days post-hatch, which are of paramount importance for vocal learning [77]; and c) *OT* mediating song preference in juveniles [54], further highlight the relevance of our *OT* findings in the song complexity differences between these two songbird species.

6. The evolution of the *OTR-VTR* genes in human and non-human primate evolution

Putting all these studies together, I realized it was high time I turned my attention back to humans to find out whether the *OT-VT* system had undergone any recent changes in humans that could speak to the behavioral differences attested between them and other non-human primates (e.g., chimpanzees, bonobos), including their ability for vocal learning, which is not present in other primates [46]. Interestingly at that time, more and more genomes of archaic humans (i.e., Neanderthals and Denisovans) were getting sequenced and becoming available for comparison in studies like ours [79–81].

I used the knowledge I had acquired in comparative genomic tools [48] and, in co-leadership with Dr. Alejandro Andirkó, we explored nucleotide variation in the *OTR-VTR* using multiple genomes of modern humans, archaic humans and non-human primates (bonobos, chimpanzees, macaques, among other species) [61]. We identified polymorphic sites with alleles (i.e., Single Nucleotide Polymorphisms) found for the first time in modern or archaic humans, or shared only between modern humans and bonobos. On these sites we performed an array of analyses (prediction, regulation, linkage disequilibrium, frequency, selection and functional association analyses) that revealed that they are located in open chromatin or transcription factor binding sites, are active in specific brain regions, and/or show positive or balancing selection signals in modern humans. Importantly, all of them were also associated with specific social behaviors and neurodevelopmental or neuropsychiatric disorders.

With these findings, we were able to shed light to specific sites that have likely been hotspots in hominin and primate evolution and could explain several of the key differences between the species studied [61] and refs. therein). For example, they might subserve sociality differences between the Pan and the Homo lineage that resulted in the decreased aggression and demographic success in the latter, or group-size differences between archaic and modern humans. The convergent sites we found in modern humans and bonobos might be relevant to similarities between them in social attention, tolerance and cooperation. Lastly, based on the gene expression patterns of the *OTR-VTR* in brain regions in humans that are associated with vocal learning [48], and based on our aforementioned findings in songbirds, it could be that the archaic and modern human-specific variants could have a synergistic heterozygous impact on the evolution of vocal learning in the human lineage.

7. Oxytocin as a treatment for speech deficits in autism spectrum disorders

Synthesizing all these findings, and considering evidence in the human literature showing that an intranasal administration of *OT* (IN-OT) alleviates several aspects of impaired socialization and communication in children with autism spectrum disorders (ASD) [82], including speech *comprehension* [83,84], I hypothesized that IN-OT could also be used to improve deficits in speech *production*. Malfunction in the *OT* system has been repeatedly linked to ASD, as we thoroughly reviewed in a book chapter [62] I co-led with Dr. Amelie Borie (Emory University), while, interestingly, aberrant changes in the *OT* or *OTR* genotype, blood genome methylation, and plasma levels have been found in ASD patients in conjunction with speech production disorders [85,86].

As an Associate Research Professor, directing the Neurobiology of Social Communication Lab at City University of New York and Rockefeller University, I was recently able to secure funding (Robertson Therapeutic Development Fund from the Rockefeller University) that will enable us to test this hypothesis in children diagnosed with ASD and speech production deficits. At this point, I am feeling that my research comes full circle, as I am finally able to address in humans the hypothesis I had put forward several years ago. Seen from a distance, the oxytocin journey has so far equipped me with great experience in different fields, including neuroscience, comparative genomics and population genetics, whose tools have been valuable in my transition to human studies, where I also apply my early knowledge in linguistics.

8. The neurobiology of dance … and oxytocin

In other scientific endeavors, I have also widened my research scope to include the study of another sensorimotor behavior that serves social communication in humans: dance [87]. Studying dance came as a necessary ramification from studying speech: evidence from different levels of analysis points to intriguing commonalities between vocal learning (i.e., speech) and beat synchronization (i.e., dance) that go beyond the fact that both behaviors rely on rhythmic motor control and on a tight auditory to motor integration. For example, only vocal learners (humans and parrots, in particular) have been found to be able to synchronize their body movements to the beat of sound in music [88], while developmental behavioral studies in human children have shown that the development of the ability for a sustained beat perception and synchronization predicts the development for phonological (speech) production ability until late childhood [89]. These and other findings have led to the hypothesis [88,90] that vocal learning was a prerequisite for the evolution of the ability to synchronize to a beat, a core feature of dance.

In the projects I am currently coordinating, we are planning to unravel the relationship between speech and dance in humans, at the level of brain pathways, gene expression, gene variants, and therapy. For the latter, we are testing the effect of a behavioral dance intervention in the speech deficits of people with Parkinson's Disease. Thinking back of the moment I saw the Erasmus advertisement for studying in Seville, and flamenco being one of the major drivers of my decision to pursue this application, I can see how my life comes full circle not only through oxytocin, but also through dance. I had never imagined it, but scientific findings would actually bring my two passions together: speech and dance.

What is even more intriguing is that the *OT-VT* system was recently found to be implicated in dance as well. In one experiment, partners while dancing together were administered intranasally either *OT* or placebo, and a motion tracking software was used to measure synchrony between them as manifested in the velocity of their movements [91]. IN-OT was found to increase synchronized interpersonal movement during dance. In another experiment, they compared the *VTR1A/AVPR1A* (vasotocin receptor 1A/arginine vasopressin receptor 1 A) between performing dancers vs. elite athletes and nondancers/nonathletes and showed significant differences in allele frequencies [92]. These findings suggest a role of *OT* and *VT* beyond speech, in the coordination of complex sensory-motor behaviors. A combined dance and oxytocin therapy to alleviate speech and general body movement deficits might be where I predict to find my research in some years from now.

9. Challenges and solutions

In this scientific and personal journey, I faced varying challenges. Some of them were specific to my trajectory, as I decided to switch fields and continuously get immersed in new tools in different species. Other challenges were (and still are) more systemic. Being a woman in science and surviving in a male-dominant environment, especially as I am progressing towards research independence, is a challenge by itself. To me it took different shapes, from being actively belittled from male colleagues to receiving verbal and physical advances and harassment. Other challenges have been pertinent to my identity as an international scholar, which include working in cultural and linguistic environments that are different to those I grew up, paired with all the relevant legal hassle (for example, to maintain, in the US, a VISA and medical insurance) and, of course, being away from the safety net of family.

I have been progressively learning how to mentally frame and overcome these challenges. For changing fields, I can only say I devoted a great deal of time in self-learning, reading, trying, and failing.

Especially in the beginning it was very difficult to fail, but then I learnt to see it as part of the process. In this, psychotherapy played a pivotal role in cracking my past wide open, in giving me practice on how to speak and how to listen. I envisage a future where psychotherapy would be readily available at no cost to all scientists. As I mentioned in the beginning of the article, dance (flamenco) has always been there to give me beat and pace whenever I felt I had lost it, but also to just help me express myself and have fun. Another artistic expression that has been life-changing is poetry. Writing a good poem gives me a feeling of fulfillment and purpose. Moving to the US prompted me to start writing in English, and my first publications in US-based poetry journals have been reinvigorating. Giving back to the community is another way for me to face my own challenges: unless we actively seek to make science and academia a diverse and equitable place, my challenges will be faced unaltered by the future generations. Last but not least, it has always been of outmost help to maintain a circle of people with whom I felt I could truly be myself, feel accepted, learn, change, listen and be listened.

Declaration of competing interest

The author has no competing interest to declare.

References

[1] Constantina Theofanopoulou, Brain asymmetry in the white matter making and globularity, Front. Psychol. 6 (2015) 1355. http://journal.frontiersin.org/Article/10.3389/fpsyg.2015.01355/abstract.

[2] Constantina Theofanopoulou, Light verbs in modern Greek, Studies in Greek Linguistics (35) (2015) 607–631.

[3] C. Núñez, et al., A large-scale study on the effects of sex on gray matter asymmetry, Brain Struct. Funct. 223 (1) (2018).

[4] Constantina Theofanopoulou, "Implications of oxytocin in human linguistic cognition: from genome to phenome.", Front. Neurosci. 10 (2016). http://journal.frontiersin.org/Article/10.3389/fnins.2016.00271/abstract.

[5] Jan Bakos, Annamaria Srancikova, Tomas Havranek, Zuzana Bacova, Molecular mechanisms of oxytocin signaling at the synaptic connection, Neural Plast. 2018 (2018), 4864107.

[6] H. Sophie Knobloch, Valery Grinevich, Evolution of oxytocin pathways in the brain of vertebrates, Front. Behav. Neurosci. 8 (February) (2014) 1–13. http://journal.frontiersin.org/article/10.3389/fnbeh.2014.00031/abstract.

[7] Andreas Meyer-Lindenberg, Gregor Domes, Peter Kirsch, Markus Heinrichs, Oxytocin and vasopressin in the human brain: social neuropeptides for translational medicine, Nat. Rev. Neurosci. 12 (9) (2011) 524–538, https://doi.org/10.1038/nrn3044.

[8] Constantina Theofanopoulou, Reconstructing the evolutionary history of the oxytocin and vasotocin receptor gene family: insights on whole genome duplication scenarios, Dev. Biol. 479 (2021) 99–106. https://linkinghub.elsevier.com/retrieve/pii/S0012160621001755.

[9] Constantina Theofanopoulou, Universal nomenclature for oxytocin–vasotocin ligand and receptor families, Nature 592 (7856) (2021) 747–755. http://www.nature.com/articles/s41586-020-03040-7.

[28] Bianca J. Marlin, et al., Oxytocin enables maternal behaviour by balancing cortical inhibition, Nature 520 (7548) (2015) 499–504.

[29] James D. Klatt, James L. Goodson, Oxytocin-like receptors mediate pair bonding in a socially monogamous songbird, Proc. Biol. Sci. 280 (1750) (2013).

[30] James L. Goodson, Laura Lindberg, Paul Johnson, Effects of central vasotocin and mesotocin manipulations on social behavior in male and female zebra finches, Horm. Behav. 45 (2) (2004) 136–143. http://linkinghub.elsevier.com/retrieve/pii/S0018506X03002381.

[40] Constantina Theofanopoulou, "Self-Domestication in Homo sapiens: insights from comparative genomics" ed. Michael klymkowsky, PLoS One 12 (10) (2017), e0185306. https://dx.plos.org/10.1371/journal.pone.0185306. (Accessed 14 February 2022).

[41] Patricia K. Kuhl, Feng-Ming Tsao, Huei-Mei Liu, Foreign-Language experience in infancy: effects of short-term exposure and social interaction on phonetic learning, Proc. Natl. Acad. Sci. U. S. A. 100 (15) (2003) 9096–9101.

[42] Y. Takayanagi, et al., Pervasive social deficits, but normal parturition, in oxytocin receptor-deficient mice, Proc. Natl. Acad. Sci. USA 102 (44) (2005) 16096–16101. http://www.pnas.org/cgi/doi/10.1073/pnas.0505312102.

[43] J.T. Winslow, T.R. Insel, The social deficits of the oxytocin knockout mouse, Neuropeptides 36 (2–3) (2002) 221–229. https://linkinghub.elsevier.com/retrieve/pii/S0143417902909091.

[44] Mariela Mitre, et al., A distributed network for social cognition enriched for oxytocin receptors, J. Neurosci. 36 (8) (2016) 2517–2535. https://www.jneurosci.org/lookup/doi/10.1523/JNEUROSCI.2409-15.2016.

[45] Vincent M. Janik, Peter J.B. Slater, in: "Vocal Learning in Mammals.", 1997, pp. 59–99. http://linkinghub.elsevier.com/retrieve/pii/S0065345408603770.

[46] Erich D. Jarvis, Learned birdsong and the neurobiology of human language, Ann. N. Y. Acad. Sci. 1016 (1) (2004) 749–777, 10.1196/annals.1298.038.

[47] Constantina Theofanopoulou, Implications of Oxytocin in Speech, University of Barcelona, 2019. http://hdl.handle.net/10803/666660.

[48] Constantina Theofanopoulou, Cedric Boeckx, Erich D. Jarvis, A hypothesis on a role of oxytocin in the social mechanisms of speech and vocal learning, Proc. Biol. Sci. 284 (1861) (2017), 20170988. https://royalsocietypublishing.org/doi/10.1098/rspb.2017.0988. (Accessed 14 February 2022).

[49] Cary H. Leung, et al., Neural distribution of vasotocin receptor MRNA in two species of songbird, Endocrinology 152 (12) (2011) 4865–4881. https://academic.oup.com/endo/article-lookup/doi/10.1210/en.2011-1394.

[50] Constantina Theofanopoulou, Erich D. Jarvis, Reply to: the case for standardizing gene nomenclature in vertebrates, Nature 614 (7948) (2023) E33–E36. https://www.nature.com/articles/s41586-022-05634-9.

[51] W.J. Kent, BLAT—The BLAST-like alignment tool, Genome Res. 12 (4) (2002) 656–664. http://www.genome.org/cgi/doi/10.1101/gr.229202.

[52] Robert C. Froemke, Larry J. Young, Oxytocin, neural plasticity, and social behavior, Annu. Rev. Neurosci. 44 (1) (2021) 359–381. https://www.annualreviews.org/doi/10.1146/annurev-neuro-102320-102847.

[53] Kengo Inada, et al., Plasticity of neural connections underlying oxytocin-mediated parental behaviors of male mice, Neuron 110 (12) (2022) 2009–2023, e5, https://linkinghub.elsevier.com/retrieve/pii/S089662732200304X.

[54] Natalie R. Pilgeram, et al., Oxytocin receptor antagonism during early vocal learning reduces song preference and imitation in zebra finches, Sci. Rep. 13 (1) (2023) 6627. https://www.nature.com/articles/s41598-023-33340-7.

[55] Zegni Triki, Katie Daughters, K. Carsten, W. De Dreu, Oxytocin has 'tend-and-defend' functionality in group conflict across social vertebrates, Phil. Trans. Biol. Sci. 377 (1851) (2022). https://royalsocietypublishing.org/doi/10.1098/rstb.2021.0137.

[56] Arang Rhie, et al., Towards complete and error-free genome assemblies of all vertebrate species, Nature 592 (7856) (2021) 737–746. http://www.nature.com/articles/s41586-021-03451-0.

[57] Alina M. Sartorius, Rokicki Jaroslav, Bettella Francesco, barth claudia, de Lange Ann-Marie G, Haram Marit, Shadrin Alexey, et al., An evolutionary timeline of the oxytocin signaling pathway, OSF Preprints (2023), https://doi.org/10.31219/osf.io/42b8g.

[58] Justin G. Meyerowitz, et al., The oxytocin signaling complex reveals a molecular switch for cation dependence, Nat. Struct. Mol. Biol. 29 (3) (2022) 274–281. https://www.nature.com/articles/s41594-022-00728-4.

[59] Eric R. Schuppe, et al., Oxytocin-like receptor expression in evolutionarily conserved nodes of a vocal network associated with male courtship in a teleost fish, J. Comp. Neurol. 530 (6) (2022) 903–922. https://onlinelibrary.wiley.com/doi/10.1002/cne.25257.

[60] Sandra Trigo, Paulo A. Silva, Gonçalo C. Cardoso, Marta C. Soares, Effects of mesotocin manipulation on the behavior of male and female common waxbills, Physiol. Behav. 267 (2023), 114226. https://linkinghub.elsevier.com/retrieve/pii/S0031938423001518.

[61] Constantina Theofanopoulou, Alejandro Andirkó, Cedric Boeckx, Erich D. Jarvis, Oxytocin and vasotocin receptor variation and the evolution of human prosociality, Comprehensive Psychoneuroendocrinology 11 (2022), 100139. https://linkinghub.elsevier.com/retrieve/pii/S2666497622000303.

[62] Amelie M. Borie, Constantina Theofanopoulou, Elissar Andari, The promiscuity of the oxytocin–vasopressin systems and their involvement in autism spectrum disorder, in: Salehi Ahmad, Dick F. Swaab, Ruud M. Buijs, Felix Kreier, Paul J. Lucassen (Eds.), The Human Hypothalamus: Neuropsychiatric Disorders, 2021, pp. 121–140. https://linkinghub.elsevier.com/retrieve/pii/B9780128199732000095.

[63] Fiona M. McCarthy, et al., The case for standardizing gene nomenclature in vertebrates, Nature 614 (7948) (2023) E31–E32. https://www.nature.com/articles/s41586-022-05633-w.

[64] Susumu Ohno, in: Evolution by Gene Duplication, Springer-Verlag, New York, 1970.

[65] K. Schughart, C. Kappen, F.H. Ruddle, Duplication of large genomic regions during the evolution of vertebrate homeobox genes, Proc. Natl. Acad. Sci. USA 86 (18) (1989) 7067. LP – 7071, http://www.pnas.org/content/86/18/7067.abstract.

[66] Austin L. Hughes, Phylogenies of developmentally important proteins do not support the hypothesis of two rounds of genome duplication early in vertebrate history, J. Mol. Evol. 48 (5) (1999) 565–576, https://doi.org/10.1007/PL00006499.

[67] Andrew Martin, Is tetralogy true? Lack of support for the 'one-to-four rule, Mol. Biol. Evol. 18 (1) (2001) 89–93, https://doi.org/10.1093/oxfordjournals.molbev.a003723.

[68] Yufeng Wang, Xun Gu, Evolutionary patterns of gene families generated in the early stage of vertebrates, J. Mol. Evol. 51 (1) (2000) 88–96, https://doi.org/10.1007/s002390010069.

[69] Xiaowei Song, Yezhong Tang, Yajun Wang, Genesis of the vertebrate FoxP subfamily member genes occurred during two ancestral whole genome duplication events, Gene 588 (2) (2016) 156–162.

[70] Seongsik Yun, et al., Prevertebrate local gene duplication facilitated expansion of the neuropeptide GPCR superfamily, Mol. Biol. Evol. 32 (11) (2015) 2803–2817.

[71] Erich D. Jarvis, et al., For whom the bird sings, Neuron 21 (4) (1998) 775–788. http://linkinghub.elsevier.com/retrieve/pii/S0896627300805942.

[72] K. Washio, Enigma of Bengalese Finches, Kindai-Bungei-sya, Tokyo, 1996.

[73] N. Taka-Tsukasa, Companion Birds, Shoka-Bo, Tokyo, 1917.

[74] Eri Honda, Kazuo Okanoya, Acoustical and syntactical comparisons between songs of the white-backed munia (Lonchura striata) and its domesticated strain, the bengalese finch (Lonchura striata var. Domestica), Zool. Sci. 16 (2) (1999) 319–326. http://www.bioone.org/doi/abs/10.2108/zsj.16.319.

[75] Yasuko Tobari, et al., Oxytocin variation and brain region-specific gene expression in a domesticated avian species, Gene Brain Behav. 21 (2) (2022). https://onlinelibrary.wiley.com/doi/10.1111/gbb.12780.
[76] Jun Li, et al., Chromatin remodeling gene EZH2 involved in the genetic etiology of autism in Chinese han population, Neurosci. Lett. 610 (2016) 182–186. https://linkinghub.elsevier.com/retrieve/pii/S0304394015302366.
[77] Alba Vicario, et al., Genoarchitecture of the extended amygdala in zebra finch, and expression of FoxP2 in cell corridors of different genetic profile, Brain Struct. Funct. 222 (1) (2017) 481–514. http://link.springer.com/10.1007/s00429-016-1229-6.
[78] Matthew T. Davis, et al., Expression of oxytocin receptors in the zebra finch brain during vocal development, Developmental Neurobiology 82 (1) (2022) 3–15. https://onlinelibrary.wiley.com/doi/10.1002/dneu.22851.
[79] Martin Kuhlwilm, others, Ancient gene flow from early modern humans into eastern Neanderthals, Nature 530 (7591) (2016) 429–433, https://doi.org/10.1038/nature16544.
[80] Matthias Meyer, others, A high-coverage genome sequence from an archaic denisovan individual, Science 338 (6104) (2012) 222–226. http://science.sciencemag.org/content/338/6104/222.
[81] Kay Prüfer, others, A high-coverage neandertal genome from vindija cave in Croatia, Science (2017). http://science.sciencemag.org/content/early/2017/10/04/science.aao1887.
[82] Guastella, J. Adam, et al., Intranasal oxytocin improves emotion recognition for youth with autism spectrum disorders, Biol. Psychiatr. 67 (7) (2010) 692–694. https://linkinghub.elsevier.com/retrieve/pii/S0006322309011226.
[83] Eric Hollander, et al., Oxytocin increases retention of social cognition in autism, Biol. Psychiatr. 61 (4) (2007) 498–503. http://linkinghub.elsevier.com/retrieve/pii/S0006322306007293.
[84] Michaela Pfundmair, Franziska Lamprecht, M. Florentine, von Wedemeyer, Dieter Frey, Your word is my command: oxytocin facilitates the understanding of appeal in verbal communication, Psychoneuroendocrinology 73 (2016) 63–66. https://linkinghub.elsevier.com/retrieve/pii/S0306453016304590.
[85] Jolien Rijlaarsdam, et al., Prenatal stress exposure, oxytocin receptor gene (OXTR) methylation, and child autistic traits: the moderating role of OXTR Rs53576 genotype, Autism Res. 10 (3) (2017) 430–438. https://onlinelibrary.wiley.com/doi/10.1002/aur.1681.
[86] Hong-Feng Zhang, et al., Plasma oxytocin and arginine-vasopressin levels in children with autism spectrum disorder in China: associations with symptoms, Neurosci. Bull. 32 (5) (2016) 423–432. http://link.springer.com/10.1007/s12264-016-0046-5.
[87] Constantina Theofanopoulou, "Mobile brain imaging in butoh dancers: from rehearsals to public performance.", bioRxiv (2023), 2023.02.26.530087, http://biorxiv.org/content/early/2023/02/26/2023.02.26.530087.abstract.
[88] Aniruddh D. Patel, John R. Iversen, Micah R. Bregman, Irena Schulz, Experimental evidence for synchronization to a musical beat in a nonhuman animal, Curr. Biol. 19 (10) (2009) 827–830. https://linkinghub.elsevier.com/retrieve/pii/S0960982209008902.
[89] Karli M. Nave, Joel S. Snyder, Erin E. Hannon, Sustained Musical Beat Perception Develops into Late Childhood and Predicts Phonological Abilities." Developmental Psychology, 2023 getdoi.cfm?doi=10.1037/dev0001513.
[90] Jao Keehn, R. Joanne, John R. Iversen, Irena Schulz, Aniruddh D. Patel, Spontaneity and diversity of movement to music are not uniquely human, Curr. Biol. 29 (13) (2019) R621–R622. https://linkinghub.elsevier.com/retrieve/pii/S0960982219306049.
[91] Liad Josef, et al., The oxytocinergic system mediates synchronized interpersonal movement during dance, Sci. Rep. 9 (1) (2019) 1894. https://www.nature.com/articles/s41598-018-37141-1.
[92] Rachel Bachner-Melman, et al., "AVPR1a and SLC6A4 gene Polymorphisms are associated with creative dance performance" ed. Jonathan flint, PLoS Genet. 1 (3) (2005) e42. https://dx.plos.org/10.1371/journal.pgen.0010042.

Further reading

[10] A.N.A. Verty, J.R. McFarlane, I.S. McGregor, P.E. Mallet, Evidence for an interaction between CB1 cannabinoid and oxytocin receptors in food and water intake, Neuropharmacology 47 (4) (2004) 593–603.
[11] Patrice Arthur, et al., "Relationship between gene expression and function of uterotonic systems in the rat during gestation, uterine activation and both term and preterm labour.", J. Physiol. 586 (24) (2008) 6063–6076.
[12] S.S. Marroni, et al., Neuroanatomical and cellular substrates of hypergrooming induced by microinjection of oxytocin in central nucleus of amygdala, an experimental model of compulsive behavior, Mol. Psychiatr. 12 (12) (2007) 1103–1117.
[13] Marek Jankowski, et al., Oxytocin in cardiac ontogeny, Proc. Natl. Acad. Sci. U. S. A. 101 (35) (2004) 13074–13079.
[14] Gareth Leng, Simone L. Meddle, Alison J. Douglas, Oxytocin and the maternal brain, Curr. Opin. Pharmacol. 8 (6) (2008) 731–734.
[15] Thomas R. Insel, Terrence J. Hulihan, A gender-specific mechanism for pair bonding: oxytocin and partner preference formation in monogamous voles, Behav. Neurosci. 109 (4) (1995) 782–789.
[16] Diane M. Witt, Thomas R. Insel, Increased fos expression in oxytocin neurons following masculine sexual behavior, J. Neuroendocrinol. 6 (1) (1994) 13–18, 10.1111/j.1365-2826.1994.tb00549.x. (Accessed 14 January 2020).
[17] Oliver J. Bosch, et al., "Brain oxytocin correlates with maternal aggression: link to anxiety.", J. Neurosci. 25 (29) (2005) 6807–6815.
[18] A. Larrazolo-López, et al., Vaginocervical stimulation enhances social recognition memory in rats via oxytocin release in the olfactory bulb, Neuroscience 152 (3) (2008) 585–593.
[19] Maria Petersson, Pawel Alster, Thomas Lundeberg, Kerstin Uvnäs-Moberg, Oxytocin causes a long-term decrease of blood pressure in female and male rats, Physiol. Behav. 60 (5) (1996) 1311–1315.
[20] S.K. Elabd, et al., Possible neuroendocrine role for oxytocin in bone remodeling, Endocr. Regul. 41 (4) (2007) 131–141. http://www.ncbi.nlm.nih.gov/pubmed/18257653. (Accessed 14 January 2020).
[21] Magalhaes, K.R.S. Joyce, et al., Oxytocin pretreatment decreases oxytocin-induced myometrial contractions in pregnant rats in a concentration-dependent but not time-dependent manner, Reprod. Sci. 16 (5) (2009) 501–508.
[22] Chiu Lung Wu, et al., Pharmacological effects of oxytocin on gastric emptying and intestinal transit of a non-nutritive liquid meal in female rats, Naunyn-Schmiedeberg's Arch. Pharmacol. 367 (4) (2003) 406–413.
[23] Jun Yang, et al., Effect of oxytocin on acupuncture analgesia in the rat, Neuropeptides 41 (5) (2007) 285–292.
[24] G.F. Jirikowski, J.D. Caldwell, C.A. Pedersen, W.E. Stumpf, Estradiol influences oxytocin-immunoreactive brain systems, Neuroscience 25 (1) (1988) 237–248.
[25] Nicholas H. Putnam, et al., The amphioxus genome and the evolution of the chordate karyotype, Nature 453 (7198) (2008) 1064–1071.
[26] Michael Lukas, et al., The neuropeptide oxytocin facilitates pro-social behavior and prevents social avoidance in rats and mice, Neuropsychopharmacology 36 (11) (2011) 2159–2168.
[27] S. Filippi, et al., Role of oxytocin in the ejaculatory process, J. Endocrinol. Invest. 26 (3 Suppl) (2003) 82–86. http://www.ncbi.nlm.nih.gov/pubmed/12834028. (Accessed 14 January 2020).
[31] H. Jonaidi, M.M. Oloumi, D.M. Denbow, Behavioral effects of intracerebroventricular injection of oxytocin in birds, Physiol. Behav. 79 (4–5) (2003) 725–729.
[32] James L. Goodson, Sara E. Schrock, Marcy A. Kingsbury, Oxytocin mechanisms of stress response and aggression in a territorial finch, Physiol. Behav. 141 (2015) 154–163.
[33] John L. Carr, Martha Ann Messinger, George M. Patton, " nesting behavior in three-toed box turtles (Terrapene carolina triunguis) following oxytocin-induced oviposition .", Chelonian Conserv. Biol. 7 (1) (2008) 124–128.
[34] Jean-Luc, Rego Do, et al., Vasotocin and mesotocin stimulate the biosynthesis of neurosteroids in the frog brain, J. Neurosci. 26 (25) (2006) 6749–6760.
[35] James L. Goodson, Andrew H. Bass, Forebrain peptides modulate sexually polymorphic vocal circuitry, Nature 403 (6771) (2000) 769–772. http://www.nature.com/articles/35001581. (Accessed 14 January 2020).
[36] James L. Goodson, Andrew K. Evans, Andrew H. Bass, Putative isotocin distributions in sonic fish: relation to vasotocin and vocal-acoustic circuitry, J. Comp. Neurol. 462 (1) (2003) 1–14, 10.1002/cne.10679. (Accessed 14 January 2020).
[37] Fernanda Francine Zimmermann, Vidarte Gaspary Karina, Maria Siebel Anna, Carla Denise Bonan, Oxytocin reversed MK-801-induced social interaction and aggression deficits in zebrafish, Behav. Brain Res. 311 (2016) 368–374.
[38] Caroline L. Wee, et al., Zebrafish oxytocin neurons drive nocifensive behavior via brainstem premotor targets, Nat. Neurosci. 22 (9) (2019) 1477–1492.
[39] Pai Chung Gwee, Boon Hui Tay, Sydney Brenner, Byrappa Venkatesh, Characterization of the neurohypophysial hormone gene loci in elephant shark and the Japanese lamprey: origin of the vertebrate neurohypophysial hormone genes, BMC Evol. Biol. 9 (1) (2009) 1–15.