Neurotrophins and their receptors distribution in the central nervous system of the Zebrafish (*Danio rerio*) - a review

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Abstract
Neurotrophins (NTs) and their receptors have been extensively studied in the last years due to their involvement in the development of the nervous system, its plasticity and survival, as well as in psychiatric or neurodegenerative diseases. In zebrafish, the popular animal model for genetic studies, recent publications reveal the localization of NTs and tyrosine kinase receptors (Trks) in most important regions of the central nervous system (CNS) of developing embryo, the distribution of brain derivated neurotrophic factor (BDNF), nerve growth factor (NGF) and TrkB in adult zebrafish brain and also the expression of main NTs and Trk receptors in the cerebellum, meanwhile some unknown pathways of the complex mapping of tyrosine kinase (Ntrk) receptors and their ligands remain to be established.
Keywords: *Zebrafish (Danio rerio), neurotrophins, Trks, p75, CNS*

Introduction

The evolutionary history of NTs and their receptors is different and complex for vertebrates. Meanwhile every NT is expressed by a single gene in all species, the Trks present a more complex organization. Due to several genome duplications that occurred during evolution, the generation of the teleost-specific NT-6/7 and duplicated TrkB and TrkC took place. This happened during the teleost specific genome duplication, when lineage-specific gene losses lead to the formation of an additional fifth member of the Nts family (NT-6/7) and also to the amplification of the Trks genes to a number of five coding genes: TrkA, TrkB1, TrkB2, TrkC1 and TrkC2. The presence of a single copy of the TrkA receptor would suggest that a second paralogue has been lost across evolution (Ohno, 1970; Ohno, 1993; Nillson et al., 1998).

The NTs are proteins first synthetized as precursors (proNTs), after that being cleaved to the mature form, the biologically active one. The proNTs and the mature NTs play both autocrine and paracrine functions. Their roles are manifold in developing and adult zebrafish, not only in the neural tissue, but also in other types of tissues, like cardiac, pulmonary, skeletal, pancreatic, hepatic, adipose tissues, or vascular, hematopoietic and immune system. In nervous system, they are involved in several characteristics of developing and mature neuronal phenotypes, including survival, proliferation and synaptic plasticity not only for the central, but also for the peripheral nervous system (Chao, 2003; Panula et al., 2010; Fontana et al., 2018).

The genomic organization of all NTs is similar. The mature protein, which is a basic peptide of approximately 120 amino acids, is synthesised by proteolytic cleavage from a prepropeptide encoded by one large exon. This coding exon is preceded by several smaller exons. Usage of different promoters and alternative splicing generates alternative 5' untranslated regions (UTRs) of mRNA. This pattern of expression generates different transcripts for the NTs genes (Dethleffsen et al., 2003).

The 4 known vertebrate NTs: NGF, BDNF, NT-3 and NT-4/5 share a structural identity of about 50%. Comparing the sequences of several vertebrate NTs showed that only about 35 amino acids are invariant, indicating that they are important for all NTs (Hallbook, 1999).

They activate two types of transmembrane receptors: the common receptor p75, a member of the tumor necrosis factor (TNF) receptor superfamily that binds all NTs with similar affinity, and a family of tyrosine kinase receptors, the so-called Trk receptors. Each NT binds preferentially to a specific Trk receptor: NGF binds to TrkA, BDNF, and NT-4/5 activate TrkB, and NT-3 preferentially activates TrkC (Kaplan and Miller, 2000; Lee et al., 2001).

In zebrafish, Martin et al. (1995) identified 5 distinct Trks: one TrkA gene, two TrkB genes- TrkB1 and TrkB2 and other two TrkC genes- TrkC1, respectively TrkC2. The detection of these receptors as Trk family members was based on their kinase regions and the structure of their extracellular regions, which contain the two cysteine clusters, leucine- rich structure and two immunoglobulin- related domains which are typical of vertebrate Trk receptors. Each of the five genes was found to be differentially expressed in the brain of developing zebrafish, suggesting that they are functionally distinct (Martin et al., 1995).

The Trk receptors are required for neurite outgrowth and cell survival. Binding of NTs to members of the Trk family produces biological responses through activation of the tyrosine-kinase domain, resulting in a rapid increase in the phosphorylation of selective cellular substrates (Chao & Hempstead, 1995).

The p75 receptor contains four negatively-charged cysteine-rich extracellular repeats, and a unique cytoplasmic domain that is highly conserved among species. There are no sequence similarities between the two receptors in either ligand-binding or cytoplasmic domains (Chao & Hempstead, 1995).

In human, cells that are responsive to NGF are quite restricted, as opposed to the more numerous neuronal populations that are dependent upon BDNF, NT-3 and NT-4/5. During development, expression of trkA is limited to sensory and sympathetic neurons in the peripheral nervous system and cholinergic neurons of the basal forebrain, while more extensive central nervous system expression is found for trkB and trkC. The p75 neurotrophin receptor has a much wider distribution and is expressed on numerous cell types, including Schwann cells, motor neurons, meningeal, dental pulp cells, hair-follicle cells, and cerebellar Purkinje cells. The widespread pattern of expression of p75 is consistent with its role as a potential receptor for BNDF, NT-3 or NT-4/5, in addition to NGF. Furthermore, the majority of NGF-responsive cells express both p75 and TrkA, in contrast to cells that express TrkB or TrkC and that might express significant levels of p75. Although p75 and trk receptors are co-expressed in many cells, independent expression of p75 and of individual members of the trk family and their isoforms is also observed (Chao & Hempstead, 1995).

In a study from 2016, a Western blot analysis of the adult zebrafish whole brain revealed the presence of NGF, BDNF, NT-3 and NT-4 proteins, together with their Trk receptors in the CNS. The NGF antibody recognized a band of approx. 25 kD; BDNF antiserum showed two bands, respectively, approx. 14 kD and approx. 39 kD; NT-3 antibodies labeled a band of approx. 32 kD; NT-4 antibodies recognized three bands, respectively, of approx. 14 kD, approx. 28 kD, and approx. 38 kD; TrkA antiserum showed one band of approx. 145 kD; TrkB labeled two bands, respectively, of approx. 70 kD and approx. 120 kD; TrkC antiserum recognized a band of approx. 130 kD. In the cerebellum, widely distributed cellular localization has been demonstrated for all four examined NTs as well as for TrkA and TrkB, whereas TrkC was restricted in few cells and fibers of the molecular layer of the corpus cerebelli. The localization of NTs has been observed mainly in Purkinje cells, meanwhile TrkA and TrkB receptors in cells and fibers of granular and molecular layers (Gatta et al., 2016).

NTs expression patterns in developing zebrafish brain

BDNF

BDNF expression was found in discrete paired domains of neuro-ectodermal transcripts across the entire embryonic head at 24 hpf, namely in brain territories and sensory epithelia. A consistent cluster of BDNF-positive cell bodies was detected in the prospective dorsal pallium of the telencephalon, a brain subdivision that at this stage can be visualized by the position of the anterior intraencephalic sulcus. In the hypothalamus, dense staining was observed at the dorsal margin, near the supraoptic area. Posterior to the cephalic flexure, two small groups of BDNF-expressing cells were found in an area whose anatomical identity includes putative diencephalic and mesencephalic precursors. Patchy distribution of BDNF-positive neurons occurred in the ventral–lateral margin of the spinal cord. Weak BDNF expression was observed in the pituitary gland, a mediator of hypothalamic signaling to the endocrine system and absent in the cerebellum (De Felice et al., 2014).

At 48 hpf, in situ hybridization of the developing brain revealed conserved and novel traits of BDNF expression. While the pallial domain remained qualitatively similar, the diencephalic pattern consisted of three major signals. Presumably, the position of the dorsal hypothalamic domain observed at 24 hpf had shifted ventrally along the anterior margin that borders the postoptic commissure. Stream of BDNF-expressing cells connected the ventral hypothalamic domain with a region of dense staining overlapping extensively with the neurosecretory preoptic area and the posterior tuberculum. A third domain of strong BDNF transcript labeling covered an area corresponding to thalamus/pretectum progenitor neurons. Low level of transcription was visible in the pituitary gland (Cacialli et al., 2016).

At 72 hpf, BDNF was markedly expressed in the central nervous system, with substantial spatial shifts. While the pallial domain and the ventral hypothalamic domain remained similar in size, position and staining intensity, BDNF was switched on in mesencephalic territories, so that a single domain encompassed posterior tuberculum, pretectum, optic tectum and putatively thalamus. Staining was still detected in olfactory bulbs and otic vesicle. Labeling was expanded towards the outer margin of the eye and towards more posterior neuromasts. Diffuse BDNF expression appeared in the pharyngeal epithelium. At 96 hpf, BDNF transcription presented a noticeable up regulation in the optic tectum. Distinct prominent signals were detected in the (caudal) pallium, ventral hypothalamus and posterior tuberculum/pretectum/optic tectum area. Moreover, a low level of diffuse in situ hybridization staining was found throughout the central nervous system (Cacialli et al., 2016).

In the brain of 7 days old larvae, BDNF was expressed in the olfactory rosettes and in the anterior telencephalon. At this level, positive cells were mostly located in the dorsal and medial parts of the dorsal telencephalon. More caudally, labeled cells were still observed in the dorsal telencephalon, preferentially in the central telencephalon and also in the preoptic area. Bdnf was particularly abundant in the thalamic area and was also consistently observed in the optic tectum, particularly in the periventricular layer. Bdnf was also detected at different levels of the midbrain tegmentum, in particular in the reticular formation (Cacialli et al., 2016).

NGF

Is expressed in the epidermis surrounding anteriorly the neural plate during early somitogenesis (12 hpf) (Thisse & Thisse, 2004, 2005). Most optic tectum cells appeared to be labeled strongly at 24 hpf. Positive cells were also observed in the ventral margin of the otic vesicle, in a small cluster of head mesenchymal cells within the pharyngeal arches, in lateral line primordium and posteriormost somites. At 36 hpf, NGF expression ceased in the optic tectum and

caudal somites, and became intense in pharyngeal arches, neurons within the trigeminal ganglion and posterior pharynx. At 48 hpf, expression persisted in the lower jaw structures, likely including the ventral oral epithelium and paired ceratobranchials, and in the posterior pharynx. No expression was observed at later stages (Nittoli et al., 2018).

NT-3

Like NGF, NT-3 expression was activated at the early somitogenesis stage (12 hpf) in the epidermis along the neural plate border, in cardiac progenitor cells and in the lateral line primordium. At 22 hpf, NT-3 positive cells were observed in the linear heart tube, otic vesicle, lateral line primordium, pancreas, and posterior somites. No sign of NT-3 expression was detected in the spinal cord. At 48 hpf, cells expressing NT-3 were present in the central retina, pituitary gland, and pancreas. No more expression was detected in lateral line and inner ear, while the cardiac signal remained ubiquitous. At 72 hpf, discrete bilateral groups of neuronal cell types expressing NT-3 were observed in the brain and cranial nerve region. Expression in the retina had spread from central to peripheral photoreceptors and to the inner nuclear layer in the temporal retina. No expression was seen at later stages (Nittoli et al., 2018).

NT-4/5

The first expression of NT-4/5 was found in the posterior epiblast during early somitogenesis (12 hpf). At 24 hpf, mRNA staining occurred in cranial nerves, lateral line primordium and in the median finfold surrounding the tail. At 48 hpf, positive cells formed columns that were arranged around the pharyngeal arch region. This signal was confined to the anterior most group of pharyngeal cells at 72 hpf. Finally, a strong signal labeled the inner wall of the intestine bulb at 96 hpf (Nittoli et al., 2018).

NT-6/7

Its developmental expression in zebrafish is unique because it was restricted to the otic vesicle. Early transcript was detected at 16 hpf in two clusters of cells adjacent to the anterior and posterior of the inner ear primordium (16 hpf). As development proceeds, NT-6/7 expression was extended in 3–4 small sensory otic vesicle patches at 24 and 48 hpf. Expression was lost at later stages (Nittoli et al., 2018).

NTs expression patterns in adult zebrafish brain

BDNF

The olfactory bulbs displayed few BDNF-positive cells in the glomerular cell layer and in the external and internal cell layers. A strong hybridization staining was observed in a large number of small round cells localized in the dorsal telencephalon particularly in its medial, lateral and posterior divisions. The ventral part of the telencephalon exhibited fewer and weakly labeled cells in the posterior zone and intensely stained cells in the entopedoncular nucleus. In the diencephalon, we observed an intense positive signal in the parvocellular, and magnocellular nuclei of the preoptic area and in the entopeduncular and suprachiasmatic nuclei. BDNF mRNAs are strongly expressed in cells of the habenula, specifically in its dorsal component and in the ventrolateral and ventromedial nuclei of the ventral thalamus, but the intensity of labeling was weaker than in the dorsal thalamic nuclei. Transcripts were also abundantly reported in the anterior, dorsal, posterior and central posterior nuclei of the dorsal thalamus. More ventrally, bdnf mRNAs were expressed in the posterior tuberal nucleus and preglomerular nuclei. In the hypothalamus, BDNF transcripts were abundantly expressed in periventricular nucleus of its ventral and dorsal part, in the diffuse and central nuclei of the inferior lobe and in the mammilary body. Between diencephalon and mesencephalon, in the so-called synencephalon, the nucleus of the medial longitudinal fascicle

displayed few BDNF -positive cells, whereas bdnf mRNAs were highly expressed in the dorsal and ventral periventricular pretectal nuclei. In the mesencephalon, BDNF mRNAs were also observed in the torus longitudinalis. The periventricular gray zone of the optic tectum exhibited numerous cells expressing bdnf trancripts. In the tegmentum, bdnf mRNA were observed in the central nucleus of the torus semicircularis and in the interpeduncular nucleus. In the medulla oblongata, BDNF mRNAs were highly expressed in the secondary gustatory nucleus and in few cells of the vagal lobe. Finally, large BDNF -positive perikarya were seen in the superior and inferior reticular formation (Cacialli et al., 2016).

NGF

The olfactory bulbs showed a moderate quantity of NGF. The cells of both external and internal cellular layers and fibers of the glomerular layer resulted positive. In the whole telencephalon, more intense NGF positivity was seen in the ventral telencephalon and in the posterior zone of dorsal telencephalic area. Positive cells were distributed in the medial, dorsal, lateral, central and posterior parts of the dorsal part of the telencephalic area. In the ventral telencephalic area, small round cells were seen in the dorsal and ventral part. Numerous intensely stained cells were seen in the anterior parvocellular preoptic nucleus and in the posterior parvocellular preoptic nucleus of diencephalon. A weak signal was detected in few cells of the magnocellular preoptic nucleus. In dorsal and ventral habenular nucleus, a few positive cells were detected. A high density of NGF-positive cells was observed in the ventro-medial and ventro-lateral thalamic nuclei. Few and weak positive cells were seen in the central posterior thalamic nucleus. Numerous positive cells were detected in the posterior tuberal nucleus. In the lateral and medial pre-glomerular nuclei, positive cells and some fibers were detected. In the hypothalamus, the ventral zone of the periventricular hypothalamus showed intense positivity in the whole-mount brain, and numerous NGF-positive cells were seen in histological sections. In the dorsal and caudal zones of periventricular hypothalamus moderate positivity was seen. Large NGF-positive cells belonging to the diffuse nucleus of the inferior lobe were seen. Few NGF-positive cells were also present in the mammillary body and in the nucleus of the medial longitudinal fascicle. Concerning the mesencephalon, NGF-positive fibers were present in the longitudinal tori and the optic tect, particularly in the deep white zone and superficial white zone. Numerous small NGF-positive cells appeared scattered in the periventricular gray zone. In the tegmentum, NGF was observed in cells of the central nucleus of semi-circular torus and superior reticular formation (Cacialli et al., 2019).

NT-3

In the cerebellum of the adult zebrafish, highly intense staining was seen in the majority of Purkinje cells of both valvula cerebelli and corpus cerebelli. Their intense positive dendrites were spread throughout the molecular layer. Only few thin positive fibers were seen in the granule cell layer (Gatta et al., 2016). Regarding NT-3 distribution in other central nervous system regions, there are no elaborate studies to date.

NT-4/5

In the Purkinje cells layer of valvula cerebelli and corpus cerebelli, strong immunoreactivity was observed in numerous Purkinje cells. The dendrites of these cells, branching in the ML, appeared intensely stained. In entire cerebellum, and especially in the granular cell layer of the corpus cerebelli, some thin positive fibers were distributed (Gatta et al., 2016. For the other areas of the adult zebrafish brain, no studies were conducted for the localization of the NT-4/5 expression.

NT-6/7

The neuroanatomical distribution of NT-6/7 in the zebrafish brain has not yet been studied. In fish, NT-6/7 expression pattern was described in adult Nothobranchius furzeri (Leggieri et al., 2019). In the olfactory bulb, numerous moderately labeled cells were found in the internal and external cellular layers, as well as in the glomerular layer. In the dorsal telencephalon, the expression pattern of NT-6/7 mRNA was characterized by weak labeling in few scattered neurons of the central nucleus, whereas intense signal probe was observed in dorso-dorsal, medial and lateral nuclei. In the ventral telencephalon, NT-6/7 mRNA weakly labeled few neurons of dorsal and lateral nuclei. In the preoptic area, NT-6/7 mRNA expression was detected in the anterior, parvo- and magnocellular nuclei, and in the suprachiasmatic nucleus. Intense staining was seen in neurons along third ventricle. In the pretectal area, strong labeling was observed in numerous neurons of cortical nucleus, as well as in neurons of parvocellular superficial pretectal nucleus. Intense staining was observed in few neurons of supraglomerular nucleus. NT-6/7 mRNA was observed in several weakly positive neurons of dorsal hypothalamus. Between forebrain and midbrain, moderate labeling was observed in neurons of the anterior glomerular nucleus, in neurons bordering the margins of the glomerular nucleus and in few large neurons in its inner part. In the longitudinal tori, NT-6/7 mRNA was intensely expressed in numerous positive neurons located mainly in the most ventral part, and along the margin with the optic tectum. In the optic tectum, positive neurons were observed in the periventricular grey zone. However, NT-6/7 mRNA expressing neurons were few in the most rostral part of the periventricular grey zone while became more numerous caudally. Furthermore, the neurons lining the margin between the optic tectum and tegmentum were intensely labeled. In the tegmentum, a positive signal was detected in neurons of layers 1, 3 and 4 of semicircular tori. Strong labeling was observed in the most rostral region of cerebellum, with scattered neurons largely diffused in the lateral nucleus of cerebellar valvula. In the most caudal part of the inferior lobe of hypothalamus, probe signal was seen in numerous small neurons of the diffuse nucleus and in large neurons of the central nucleus. NT-6/7 mRNA was moderately localized in neurons of Purkinje layer of the lateral region of the cerebellar valvula. Positive neurons in the Purkinje layer were also observed in the ventro-lateral and ventro-ventral subdivisions of cerebellar body. Few positive neurons were labeled in the cerebellar crista. In medulla oblongata, the expression pattern was seen in scattered neurons of octavolateral area, and in neurons of superior and intermediate reticular formation (Leggieri et al., 2019).

Trks expression patterns in developing zebrafish brain

TrkA

At 24 hpf, the zebrafish TrkA was expressed in two domains of cranial nerve ganglia flanking the hindbrain: a large and a small group anterior and posterior to the otic vesicle, respectively. The TrkA transcript was detected in Rohon-Beard (RB) neurons localized in the dorsal aspect of the spinal cord. At 48 and 72 hpf, TrkA -positive cells were similarly distributed as they were seen in two columns projecting toward the eye in the ventral head mesenchyme, and in trigeminal sensory neuron subtypes. Cells expressing TrkA were found at the base of the pectoral fins, suggesting a correspondence to pectoral motor nerve ganglia. No spinal cord labeling was detected at this stage (Nittoli et al., 2018). At 6 dpf, TrkA was expressed in the trigeminal ganglion and in the rostral hindbrain in a small subset of cells, but not in the Mauthner cells (Martin et al., 1995).

TrkB1

The expression of the TrkB2 gene in the trigeminal ganglia and RB neurons has been described by Martin et al. (1995) and Palanca et al. (2013). Nittoli et al. (2018) observed hypoblast labeling throughout the embryo at early somitogenesis stage (12 hpf). At 24 hpf, TrkB2 transcription occurred in discrete groups of neuronal cell types in the posterior telencephalon, hypothalamus, ventral thalamus, ventral tegmentum, ventral hindbrain, cranial ganglia, and spinal cord. Cells expressing TrkB2 in the spinal cord are RB neurons localized dorsally, as well as ventral cells that may represent motoneurons or interneurons. At 48 hpf, TrkB2 mRNA marked the brain, with new signals appearing in trigeminal ganglion and ganglion cell layer (GCL). The cerebral signal was still diffuse at the stage of 96 hpf, when strong staining was found in the pharyngeal epithelium.

In the brain of 6 dpf zebrafish, Martin et al. (1995) detected a distinct pattern for each of the two genes of TrkB. TrkB1 was found in a high percentage in the caudal hindbrain. Also in the peripheral nervous system appeared intensely expressed.

TrkB2

At 12 hpf (6 somite stage), TrkB2 mRNA was evenly localized in the anterior half of the embryo. TrkB2 was expressed in posterior telencephalon, ventrorostral thalamus, ventral tegmentum, and ventral hindbrain at 24 hpf. Hybridization staining was spread in the brain at 48 hpf, when a new expression domain appeared in the ganglion cell layer. The cerebral signal was still diffuse at 96 hpf (Nittoli et al., 2018).

A study from 2010 investigated the expression of BDNF and TrkB in the lateral line system of zebrafish during development (Germana et al., 2010). TrkB expression had the peak at 20 days, reaching values ranging from 12- to 2-fold those found in adults. Later on, the levels of expression of TrkB decreased to the very low, but detectable, expression levels found in adult animals. TrkB immunoreactivity was regularly found in most of the neuronal bodies of the anterior and posterior lateral line ganglia, which contains the neurons that innervate the neuromast of the body canal, at all the ages examined. Interestingly, expression of TrkB was not detected neither in the axons of these neurons nor in the nerve fibers supplying neuromasts. Nevertheless, in the neuromasts themselves there was a clear age dependent change in the levels of expression of TrkB. From 30 up to 50 dpf, all sensory cells were TrkB positive, whereas in adult animals (180 dpf) TrkB immunoreactivity is restricted to a few cells located at the periphery of the neuromast with faint intensity but specific immunolabeling (Germana et al., 2010).

Martin et al. (1995) found lower levels of TrkB2 in the caudal hindbrain and spinal cord compared with TrkB1. In the caudal hindbrain the expression of TrkB2 was very low or undetectable.

TrkC1

Groups of TrkC1 mRNA-positive cells were found in the telencephalon, pituitary gland, posterior hypothalamus, ventro-rostral thalamus, posterior hindbrain, cranial ganglia, otic vesicle, and RB neurons. TrkC1 was undetectable in the trigeminal ganglia. With some exceptions, TrkC1 mRNA pattern is very similar with that of ntrk2a, and even more with that of BDNF. At later developmental stages, TrkC1 expression occurred in pectoral motor nerve ganglia (48 hpf) and diffusely in the brain (48–96 hpf) (Nittoli et al., 2018).

Martin et al. (1995) found that TrkC1 and TrkC2 have a heterogeneous but different expression pattern. In the embryonic brain trkC2 is expressed in more sites than trkC1. However, each of these sites is a small region of the brain comprised of only a few cells.

24 hpf trkC1-positive cells are present in two sites whereas trkC2-positive cells are present in six sites in the brain. Both trkC1 and trkC2 are expressed in a subregion of the telencephalon, the dorsolateral portion of the caudal telencephalon. The trkC1-positive cells are located next and medially to the olfactory placode. Both TrkC1 and TrkC2 are expressed in the nucleus of the tract of the postoptic commissure. The TrkC1 gene is expressed also in the trigeminal ganglion, posterior lateral line ganglion and Rohon- Beard neurons (Martin et al., 1998).

TrkC2

Regarding the expression of TrkC2, Martin et al. (1998) found that its gene was expressed in the telencephalon, in the nucleus of the tract of the postoptic commissure, anterior hypothalamus, ventral midbrain, rhombomeres 4, 5, and 6, caudal hindbrain, and lateral spinal cord. At 24 hpf, the expression of the TrkC2 gene was confined to small groups of neural cell types in the telencephalon, ventral thalamus, ventral tegmentum, and anterior margin of the otic vesicle. This pattern was reminiscent of TrkB2 transcript distribution at same stage, raising the possibility of functional redundancy between TrkB2 and TrkC2. At 48 hpf, ntrk3b expression was switched on in the olfactory placode, GCL, and hindbrain, while it persisted in diencephalon and midbrain. Finally, TrkC2 transcription was detected across the brain at 96 hpf (Nittoli et al., 2018). Both TrkC1 and TrkC2 were expressed in the GCL at 6 dpf (Auer et al., 2015).

Trks expression patterns in adult zebrafish brain

TrkA

The neurodistribution of TrkA receptor in adult zebrafish has not been studied so far. A study from 2003 revealed a TrkA-like immunoreactivity in the olfactory sensory neurons. Thus, the crypt neurons of the olfactory epithelium displayed TrkA-like immunoreactivity in the stroma, their central processes being unreactive (Catania et al., 2003).

TrkB

A study of Abbate et al. (2014) revealed that cells displaying TrkB immunoreactivity in the encephalon of adult zebrafish were scarce. Specific immunoreactivity for TrkB was observed in different districts of zebrafish central nervous system preceding rostro-caudally: the diencephalon, mesencephalon and rhomboencephalon. In the diencephalon TrkB immunostaining was observed in the hypothalamic inferior lobe mainly in neurons localized in the caudal zone of periventricular hypothalamus surrounding the posterior recess of diencephalic ventricle. In the mesencephalon and the rhomboencephalon TrkB positive cells were also observed. They were large neurons, organized in a columnar fashion from rostral to caudal. Characteristically they showed a polarized nucleus, and large thin processes which did not branched, and the pattern of immunostaining was cytoplasmic. Based on their localization within the brainstem, their cytoarchitecture, and their morphology, the TrkB positive neurons were identified as motor neurons of the reticular formation.

TrkB2

Expression of TrkB2 in the adult zebrafish brain was observed in the dorsal telencephalon, the pallium, the parvocellular pre-optic nucleus, the posterior tuberculum, the radial glial cells lining the mesencephalic ventricle, the cerebellum, the hypothalamus, and a dispersed staining pattern in the medulla oblongata (Sahu et al., 2019).

TrkC

There are currently no studies regarding the distribution pattern of the TrkC1 and TrkC2 in the nervous system of the adult zebrafish.

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