Parvalbumin interneuron alterations in stress-related mood disorders: a systematic review

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Highlights

- In rodents, chronic stress reduces numbers of PV cells in PFC and HC and increases them in the BLA.
- Stress effects on PV cells are age-, sex-, stress recency- and region-dependent.
- Antidepressants protect from stress-induced PV cell loss.
- Translatability to humans is minimal but improving with technological advances.

Graphical Abstract

Declaration of interest: none.

Abstract

Stress-related psychiatric disorders including depression involve complex cellular and molecular changes in the brain, and GABAergic signaling dysfunction is increasingly implicated in the etiology of mood disorders. Parvalbumin (PV)-expressing neurons are fast-spiking interneurons that, among other roles, coordinate synchronous neuronal firing. Mounting evidence suggests that the PV neuron phenotype is altered by stress and in mood disorders. In this systematic review, we assessed PV interneuron alterations in psychiatric disorders as reported in human postmortem brain studies and animal models of environmental stress. This review aims to 1) comprehensively catalog evidence of PV cell function in mood disorders (humans) and stress models of mood disorders (animals); 2) analyze the strength of evidence of PV interneuron alterations in various brain regions in humans and rodents; 3) determine whether the modulating effect of antidepressant treatment, physical exercise, and environmental enrichment on stress in animals associates with particular effects on PV function; and 4) use this information to guide future research avenues. Its main findings, derived mainly from rodent studies, are that stress-related changes in PV cells are region-, age-, sex-, and stress recency-dependent, and that antidepressants protect from stress-induced PV cell loss. These observations do not currently translate well to humans, although the postmortem literature on the topic remains limited.

Keywords: Parvalbumin; stress; depression; interneuron; perineuronal nets.

In-text acronyms:

PV: parvalbumin; GABA: gamma-aminobutyric acid; PNN: perineuronal net; HC: hippocampus; PFC: prefrontal cortex; MDD: major depressive disorder; BD: bipolar disorder; BLA: basolateral amygdala; GR: glucocorticoid receptor; HPA: hypothalamic-pituitary-adrenal; OFC: orbitofrontal cortex; mPFC: medial prefrontal cortex; MS: maternal separation; LB/LN: limited bedding/limited nesting; MSEW: maternal separation-early weaning; SI: social isolation; SDPS: social defeat-prolonged stress; CVS: chronic variable stress; UCMS: unpredictable chronic mild stress; IHC: immunohistochemistry; mRNA: messenger ribonucleic acid; CA1/CA2/CA3: cornu ammonis 1/2/3; DG: dentate gyrus; PrL: prelimbic cortex; WFL: Wisteria floribunda lectin; WFA: Wisteria floribunda agglutinin; sIPSC: spontaneous inhibitory postsynaptic current; IL: infralimbic cortex; ACC: anterior cingulate cortex; qPCR: quantitative polymerase chain reaction; E/I: excitation/inhibition; mEPSC: miniature excitatory postsynaptic current; ERK: extracellular signal-related kinase; dlPFC: dorsolateral prefrontal cortex; BA9: Brodmann area 9; BA24: Brodmann area 24; TRN: thalamic reticular nucleus; FACS: flow-associated cell sorting.

1.1 Introduction

Parvalbumin (PV) neurons are a type of GABAergic interneuron defined by their expression of the calcium-binding protein parvalbumin. In the telencephalon, they can be subdivided into two types: basket cells, whose axons innervate the soma and proximal dendrites of principal cells; and chandelier cells, which synapse onto the initial axon segment of their targets (Hu et al., 2014). PV cells share common electrophysiological parameters and roles in microcircuits and are particularly implicated in plasticity and learning (Hu et al., 2014). Notably, their functional maturation controls the opening and closure of critical windows of enhanced plasticity during postnatal development (Bradshaw et al., 2018) and mature PV cells coordinate synchronous oscillatory firing of principal neurons through feed-forward inhibition (Hu et al., 2014), thereby regulating the balance of excitatory and inhibitory neurotransmission in the brain. The influence of PV cells on developmental neuroplasticity is strongly associated with the establishment of specialized condensed extracellular matrix structures called perineuronal nets (PNNs), which ensheath the somata, proximal dendrites, and initial axon segments of a large proportion of PV neurons. Among other roles, they buffer oxidative stress and regulate the formation and function of synapses by interacting directly or indirectly with neurotrophic factors, receptors, and guidance cues (Wen et al., 2018). Indeed, PNNs seem to influence every aspect of PV neuron physiology and connectivity.

Consistent with a broad implication of GABAergic interneurons in neuropsychiatric disorders (Prévot & Sibille, 2020), disruptions in PV cells in the hippocampus (HC) and prefrontal cortex (PFC) have been associated with mood disorders (Page et al., 2019b; Zaletel et al., 2016). Postmortem brain studies have revealed reductions in PV interneurons in the hippocampus and

prefrontal cortex of people with major depressive disorder (MDD) and bipolar disorder (BD) (Knable et al., 2004; Konradi et al., 2011; Rajkowska et al., 2007). These findings are consistent with findings showing the PV neurons are particularly impacted by chronic stress, a major risk factor for MDD and BD. Functional consequences of chronic stress on PV cells have been observed in many brain regions in animals, particularly in the HC (Hu et al., 2010), PFC (Wieck et al., 2013), and basolateral amygdala (BLA) (Guadagno et al., 2020). Depressed patients (Black et al., 2015; Michel et al., 2012) and individuals experiencing chronic or severe life stress (Salim, 2017; Schiavone et al., 2013) have higher levels of oxidative stress in the brain, which is negatively associated with the integrity of PV interneurons and their surrounding PNNs (Steullet et al., 2017). Further, a majority of PV interneurons in the rat infralimbic cortex express glucocorticoid receptors (GRs) whereas other interneuron populations in the region do not stain for GRs (McKlveen et al., 2019). These infralimbic PV cells show reduced GRs and increased activity following chronic stress in adults (McKlveen et al., 2016), suggesting a possible involvement of PV neurons in the disruption of the hypothalamic-pituitary-adrenal (HPA) axis' negative feedback loop in chronic stress conditions. This review examines the evidence implicating PV neurons in mood disorders, including studies conducted with animal stress models. A number of relevant parameters were taken into consideration following our literature search such as regional effects, sex, age, and various forms of environmental enrichment.

Abundant research in stress neurobiology has focused on the HC, amygdala, and PFC as they are particularly impacted by mood disorders. These three regions and communication between them are involved in cognitive and affective processes that are disturbed in mood disorders. In general, chronic stress reduces neurotrophic signaling in the HC and PFC (Liu et al., 2017; McEwen et

al., 2016), resulting in impaired plasticity and dendrite retraction, whereas the opposite trend is observed in the BLA (Boyle et al., 2013). This pattern may underlie the cognitive and mood changes in depression; depressed patients and rodents displaying depressive-like behavior commonly show impaired executive function, learning, and memory, processes associated with the PFC and HC, whereas behavioral inhibition and reactivity to negative stimuli, functions associated with the amygdala, are increased (McKlveen et al., 2019). Moreover, the effects of stress on neurogenesis and synaptic rewiring can be subregion-specific. For example, the orbitofrontal cortex (OFC) and medial PFC (mPFC) respond differently to stress, as do the BLA and central amygdala.

Sex-specific responses to stress have also been reported in PV neurons in animal studies; recent findings have highlighted sex-specific stress-induced PV cell transcriptomic changes (Girgenti et al., 2019) as well as changes to parvalbumin expression and cell density that associate with cognitive outcomes (Goodwill et al., 2018). Unfortunately, most of the animal stress model literature concerns male rodents; certain stress paradigms (e.g., social defeat) are more suitable to males, and females' estrus cycle and associated hormonal fluctuations can confound results (Furman et al., 2019; Milner et al., 2013; Takahashi et al., 2017). The apparent ease of research with male animals comes at a scientific cost given that mood disorders are significantly more prevalent in women than in men. Furthermore, female animals tend to exhibit different neurobiological, cognitive, and behavioral outcomes in response to stress (Galea et al., 1997; Luine et al., 2017).

Moreover, developmental timing and stress recency also play major roles in determining the neurobiological response to stress (Gee et al., 2015). Stress acts differently on the brain depending on developmental stage and interferes with neurodevelopment – typically in a deleterious manner when the stressor is highly intense or frequent. Early life stress is particularly harmful as evidenced by its position as a major predictor of later psychiatric illness. This is likely due to the brain's greater malleability in response to stimuli in youth and the potential of stressors to compromise optimal neurodevelopment. Social isolation during early-life, for example, has notable effects on neurodevelopment. While it is beyond the scope of this review to extensively describe cellular alterations associated with early-life isolation, it is worth mentioning that several studies have indicated that social isolation early in life (postweaning) alone or in combination with another stressor such as maternal separation induces changes in PV expression and function as well as in the number of PNNs (Gildawie et al., 2021; Maćkowiak et al., 2019; Ueno et al., 2017). These effects may have a lasting impact on the emergence of psychopathologies, considering that PV cells may have an important role in the neural circuitry necessary for the maturation and expression of social behavior (Bicks et al., 2020).

The recency of stressors is relevant as well; rodents and humans alike show early hyper-reactivity to stress-associated stimuli, but these reactions dull over time when the animal is returned to a more congenial environment. The neurobiological signature of this diminishing response may be reflected in PV neurons.

There is ample evidence that PV cell structure and function can be modulated by enrichment paradigms, such as antidepressant drug administration, physical exercise, and environmental

enrichment, all of which can counteract the deleterious effects of chronic stress. In this review, we included treatment with antidepressant drugs such as fluoxetine and ketamine as enrichment protocols because of their use in treating stress-related mood disorders in humans. One notable example of enrichment impacting PV neurons is that of fluoxetine's effect on PNNs; numerous studies have demonstrated chronic fluoxetine treatment to reduce the densities of PNNs and PV cells in the HC (Karpova et al., 2011; Mukhopadhyay et al., 2021), PFC (Guirado et al., 2014; Ohira et al., 2013), and BLA (Karpova et al., 2011). Making PV cell dendrites more freely accessible for the formation and elimination of synapses may be one of the mechanisms underlying the antidepressant effects of fluoxetine.

Here, we systematically review the literature on PV interneurons in postmortem studies and animal models of mood disorders. We further include animal studies of enrichment paradigms that act as a buffer or protective influence against the behavioral and biological effects of stress. The most robust finding to emerge from animal studies is a tendency of stress-associated PV cell loss in subregions of the PFC and HC that was in some cases preventable by subjecting the animals to antidepressant or anti-inflammatory drug regimen during stress. This trend was highly heterogeneous, however, and was mainly found in males. Human postmortem studies were considerably less numerous and lacked the weight and consistency to support robust conclusions. However, a trend of reduced PV expression was observed in the dorsolateral PFC of individuals with BD.

1.2 Methods

1.2.1 Animal Stress Models

Models of early-life stress, a factor which strongly predisposes to psychopathologies, include maternal separation (MS) and limited bedding/limited nesting (LB/LN). The former involves isolating pups from their mothers for a period each day during early postnatal life and can also be combined with early weaning (MSEW). The latter involves providing mothers with insufficient bedding material to provide a nurturing environment for their pups. Models of stress administered during juvenility, adolescence and adulthood include social isolation, chronic restraint or immobilization, and chronic social defeat (Chu et al., 2016; Ieraci et al., 2016; Iñiguez et al., 2016; Murthy & Gould, 2020). Social isolation (SI) is a major risk factor for psychiatric illness in humans (Leigh-Hunt et al., 2017), and animal models mimic this by isolating rodents for periods of roughly 2 weeks to 3 months. In chronic restraint or immobilization protocols, rodents are placed in cylindrical tubes or have their limbs taped to their sides, making them unable to move for a period of each day. These interventions reliably elevate glucocorticoid levels and produce behavioral and neurobiological hallmarks of mood disorders (Chu et al., 2016; Zheng et al., 2018). Experiencing social adversity such as bullying is a risk factor for depression in humans (Björkqvist, 2001), and the chronic social defeat model aims to reproduce this in animals. In this paradigm a rodent is routinely subordinated to another in direct physical confrontations. One novel adaptation of subordination stress is the social defeat-prolonged stress (SDPS) paradigm, in which an animal is subordinated to another for five consecutive days and then socially isolated until testing. This manipulation is meant to mimic a traumatic trigger and the following lack of social support that is associated with depression (Spijker et al., 2020). Some other chronic stress paradigms used in rodents include chronic mild stress, chronic variable stress (CVS), and unpredictable chronic mild stress (UCMS) (Spijker et

al., 2020). These involve subjecting rodents to a variety of stressors, typically physical or social. Physical stressors can include restraint, tail pinches, overnight illumination, and more. Examples of social stressors are isolation, crowded housing, and social defeat (Spijker et al., 2020; Umemori et al., 2015). Maternal stress during gestation in rodents is also used to model mood disorders given robust evidence that it increases the incidence of mood disorders in children¹⁸ and produces depressive-like symptoms in animal offspring (Kim et al., 2015). Examples of stressors applied to mothers include immobilization and chronic variable stress.

1.2.2 Postmortem studies

Postmortem studies of human brains have yielded major insights into the molecular and functional manifestations of mood disorders (Bani-Fatemi et al., 2017). Brains harvested in a timely manner after death can be preserved and used for neurobiological studies. However, postmortem studies are susceptible to influence by a range of confounding factors such as postmortem interval, cause of death, history of medication, and comorbidities that make it difficult to have appropriately control-matched samples. Research groups with expertise in postmortem immunostaining and other approaches typically control for factors that may impact signal detection, such as postmortem interval, tissue pH, and autofluorescence. Further, in light of these potential shortcomings, animal models are useful complements to human brain studies, with the obvious caveat of species differences.

1.2.3 Approaches used to assess PV interneurons

Immunohistochemistry (IHC) was the primary tool used to visualize PV interneurons in studies included in this review. It was used mainly to assess the total number or density of PV cells in various brain regions. Co-staining was also used in several studies to interrogate particular

aspects of PV cell phenotype or activity. For example, c-Fos staining in PV cells was used to assess PV cell activation after a given stressor (Page et al., 2019b). Electron microscopy can provide deeper insights into cellular functions of PV neurons, including subcellular receptor localization and dendritic features. Many studies included in this review also measured the mRNA or protein expression of parvalbumin in a brain region. While these do not fully elucidate local PV neuron function in a given region, they nevertheless add a layer of understanding to PV cell physiology in stressed animals. Of note, Donato et al., reported that PV expression (measured by IHC) correlates with GABA production (Donato et al., 2013).

Reductions in PV neuron numbers and in the expression of PV protein have been observed in the HC of stressed animals (Czeh et al., 2005; Filipovic et al., 2013), and it has been debated whether these findings are due to PV cell death or to attenuated maturation. Two studies by Filipovic et al. in 2011 and 2013 appeared to favor the second hypothesis, with their reports that adulthood social isolation-associated PV cell reductions in the dentate, CA1 and CA3 HC subfields were not accompanied by increased staining for apoptotic markers such as cytosolic cytochrome c and mitochondrial p53 protein. However, a nonsignificant trend toward increased apoptotic markers in the HC in this study may indicate the contrary. Increases in oxidative stress markers have been reported in both the PFC and HC of adult socially isolated rats (Zlatković et al., 2012) and in PV neurons of maternally separated animals' dentate gyrus (DG), CA1 and prelimbic cortex (PrL) (Soares et al., 2020).

It seems that there likely is a combination of arrested development and apoptosis of PV cells, both of which may stem from a common cause of increased oxidative and excitotoxic stress in

cells that counteracts neurotrophic signaling and cell maturation and leads to apoptosis in some cases. Likewise, reductions in the expression of PV protein or mRNA in a given region may be due to either cell loss or compromised maturation, as expression of parvalbumin protein increases with PV cell differentiation. To clarify: in this paper we use the wordings “PV cell loss” and “reduction in PV cell number or density” interchangeably, and thus PV cell loss will not specifically refer to cell death.

Electrophysiological recordings of PV cells or pyramidal neurons onto which they synapse can be used to yield insights into PV cell function. PV neurons coordinate oscillatory neuronal firing at theta frequency in local microcircuits in the mouse hippocampus, and optogenetically silencing them disrupts theta rhythm³. PV cells have a unique electrophysiological signature, and thus their signaling onto pyramidal neurons can be gleaned by measuring spontaneous inhibitory postsynaptic currents (sIPSCs) on pyramidal neuron plasma membranes. Excitability can be evaluated by recording PV cells directly or sIPSCs on pyramidal neurons in response to current injection, chemogenetic or optogenetic stimulation, or drug administration.

Specialized extracellular matrix structures called perineuronal nets (PNNs) commonly ensheath PV neurons (Wen et al., 2018). PNNs serve various functions, including regulating synaptic transmission by interacting with neurotrophins, transcription factors, and cell surface molecules such as receptors, protecting their ensheathed neurons from oxidative stress, and regulating synaptic plasticity (Berretta et al., 2015; Wen et al., 2018). PNNs are established during postnatal development and their maturation is intimately associated with the opening and closure of critical periods of enhanced neuroplasticity (Wen et al., 2018). Recent evidence suggests that

PNNs on PV neurons may be altered by early life stress in animals (Gildawie et al., 2019; Mukhopadhyay et al., 2021) and humans (Tanti et al., 2020), which are thought to reflect changes in PV cell excitability, plasticity, oxidative stress, and other metabolic functions (Wen et al., 2018). PNNs are typically labeled using a lectin called Wisteria floribunda lectin (WFL) or agglutinin (WFA), which binds a carbohydrate residue found in PNNs, in particular those surrounding PV neurons. This represents a shortcoming of PNN measurement, however, as WFA/WFL staining does not account for other molecular components of PNNs, some PNNs are not recognized by this lectin, and their makeup can vary according to the cell types they surround (McEwen et al., 2016), biasing the results obtained solely from WFL/WFA staining. Specific components of PNNs have been shown to control the localization of ion channels (Favuzzi et al., 2017) and to regulate axon growth (Foscarin et al., 2017), and changes to these components are not detected by WFA/WFL staining. Hopefully, in future studies other techniques such as mass spectrometry- and antibody-based detection of PNN elements, including carbohydrate residues and proteins (Konradi et al., 2011; Riga et al., 2017; Wang et al., 2018), will help to fill gaps in our understanding of PNN remodeling.

Ultimately, beyond the biological interpretation of density changes of specific cell types or changes in protein expression associated with an experimental condition or disease, methods of investigation based on immunostaining can be quantitatively flawed and prompt to bias. Tissue collection and preparation, choice of antibodies, immunolabeling protocols, and quantification all vary considerably between studies, and necessarily influence their results and interpretations. Such limitations are particularly amplified in postmortem studies, where sample preparation and quality can strongly impact the outcome of immunolabeling. Because of these limitations,

assessing PV integrity through multiple experimental approaches combining immunolabeling, gene expression, and more functional assays such as electrophysiological recordings are necessarily much more informative and should be privileged.

1.2.4 Inclusion/exclusion criteria

We conducted a search across MEDLINE, Web of Science, and Pubmed on March 24, 2020 using a search strategy outlined in the Supplementary Materials. The initial screen yielded 4141 studies after duplicates were excluded. An updated search on December 7, 2020 spanning publications in 2020 and 2021 yielded 485 non-duplicate articles. Abstracts were screened to further narrow down the field by applying the following inclusion and exclusion criteria: studies of interest 1) assessed PV interneurons 2) in postmortem brain samples from patients with mood disorders or animal models (environmental stress) of mood disorders 3) in comparison to samples from psychiatrically healthy individuals or unstressed controls, respectively. Further, control-matched animal studies examining the effects of antidepressant administration, environmental enrichment, and physical exercise interventions on PV interneurons were all included (under *enrichment*). Finally, because environmental stress models have superior construct validity in mimicking the causes of mood disorders in humans (Planchez et al., 2019), drug-induced models were excluded, including chronic administration of stress hormones such as corticosterone or inflammatory molecules such as lipopolysaccharide. A full-text information search from the resulting 168 articles yielded 129 studies that were ultimately included in this review (Fig. S1).

1.3 Results

A summary of all extracted studies can be found in Tables 1-5. For interpretation of animal studies, we grouped rodents into four age categories: early postnatal (birth to postnatal day 19 (P19)), juvenile (P20-P30), adolescent (P31-P60), and adult (P60+).

1.3.1 Changes in PV neuron populations

The majority of studies that assessed PV interneuron changes due to stress measured their density or total number in a given brain region. Immunohistochemical studies tended to show PV cell losses in subregions of the PFC and HC of stressed animals. In the PFC, while most studies reported no change in PV cell density, those in which stress did lead to a change overwhelmingly found a decrease in the prelimbic and infralimbic (IL) areas (Table 1). This trend held most strongly for adolescents, whereas adult animals showed PV cell loss in the IL but not in the PrL cortex and juveniles displayed minimal change (Brenhouse & Andersen, 2011; Clarke et al., 2019; Czeh et al., 2015; do Prado et al., 2015; Ganguly et al., 2015; Gildawie et al., 2019; Grassi-Oliveira et al., 2016; Helmeke et al., 2008; Helsin & Coutellier, 2018; Leussis et al., 2012; Lussier & Stevens, 2016; Moench et al., 2020; Ohta et al., 2020; Page & Coutellier, 2018a; Shepard et al., 2016; Soares et al., 2020; Ueno et al., 2017; Wang et al., 2019). Drug enrichment protocols protected against stress-associated PV cell loss in some studies (Ganguly et al., 2015; Todorovic et al., 2018; Wieck et al., 2013), while enrichment alone did not tend to change the number of PV cells in the PrL and IL in unstressed animals (Sampedro-Piquero et al., 2019; Song et al., 2019; Yang et al., 2015) (Table 4). A few studies stained PV cells in the anterior cingulate cortex (ACC), the mPFC, and the whole PFC, reporting mixed findings with no clear trend in any direction (Table 1). Likewise, enrichment studies produced varied effects in these regions (Jargalsaikhan et al., 2017; O'Connor et al., 2019; Todorovic et al., 2018).

As in the PFC, chronic stress paradigms tended to produce reductions in the densities of PV cells throughout the HC (Table 2). This held robustly in the dentate gyrus, CA1 and CA2/3, and inconsistently in the CA3 and whole hippocampus of adult animals, with weaker evidence suggesting decreases in adolescents as well. It was not clear how co-administration of antidepressant drugs affected the PV cell response to stress – in the dentate, while two studies found them to protect against stress-induced PV cell loss (Czeh et al., 2005; Peric et al., 2018), another reported fluoxetine combined with social isolation to reduce the number of PV cells compared to social isolation alone (Filipovic et al., 2011). Most studies of enrichment alone found no change (Anstotz et al., 2018; Gomes da Silva et al., 2010; Mukhopadhyay et al., 2021; Sampedro-Piquero et al., 2018; Serra et al., 2020; Umemori et al., 2015), with single studies finding an increase (Serra et al., 2020) and a decrease (Yang et al., 2015) in PV cells in the region. Enrichment studies in CA1 sometimes reported an increasing effect (Filipovic et al., 2013; Gomes da Silva et al., 2010; Nguyen et al., 2013; Peric et al., 2018), with one study finding a reduction (Guirado et al., 2014). Physical exercise (Peric et al., 2018; Pesarico et al., 2019; Serra et al., 2020) and antidepressants (Czeh et al., 2005; Filipovic et al., 2017; Peric et al., 2018) had increasing or stress-protective effects on CA2/3 PV cells.

In contrast to the PFC and HC, stress protocols tended to increase the number of PV cells in the BLA (Giachino et al., 2007; Gildawie et al., 2019; Manzano Nieves et al., 2020; Pesarico et al., 2019). Studies of the somatosensory cortex suggested a possible decrease in PV cell density in adolescents (Chen et al., 2018) and adults (Lee et al., 2015), although there are too few studies to draw conclusions with confidence (Table 3).

1.3.2 PV expression

Several studies quantified the expression of parvalbumin mRNA via qPCR and PV protein via Western blotting or as the intensity of IHC stains. PV expression has been shown correlate with PV cells' GABA levels and maturity (Donato et al., 2013), thus its expression provides insight into regional excitation/inhibition (E/I) balance and the local population demographics of PV cells. The general trend suggests that stress tends to decrease, rather than increase, PV protein and mRNA in the PFC of rodents in a region-dependent manner.

In the PrL cortex, stressors tended to decrease PV protein expression in adolescents rather than adults or juveniles (Brenhouse & Andersen, 2011; do Prado et al., 2015; Leussis et al., 2012; Moench et al., 2020), however this was matched by null findings (Clarke et al., 2019; Gildawie et al., 2019; Ueno et al., 2017; Ueno et al., 2018).

Most studies of the IL cortex reported no change in PV protein (Clarke et al., 2019; Gildawie et al., 2019; Soares et al., 2020; Ueno et al., 2017; Ueno et al., 2018) except one account in which MS decreased male but not female adolescent PV protein expression, an effect which was not rescued by EE after weaning (do Prado et al., 2015). One study of the OFC found that LB/LN reduced PV mRNA expression in adult males and females (Goodwill et al., 2018), hinting that PV cells in the region may be worthy of further study in the context of early life stress.

In the whole PFC, a trend suggested that animals lost PV protein or mRNA after stress (Goodwill et al., 2018; Holl et al., 2014; Lukkes et al., 2017; Lukkes et al., 2018; Schiavone et al., 2009; Sun et al., 2016), although this was not consistent (Banasr et al., 2017; Goodwill et al.,

2018; Heslin & Coutellier, 2018; Holm et al., 2011; Rossetti et al., 2018), and one research group has reported increased mRNA in stressed animals (Shepard et al., 2016; Shepard & Coutellier, 2017). PV protein and mRNA expression were unchanged by an enrichment protocol alone (Schiavone et al., 2009; Sun et al., 2016) and when combined with a chronic stress regimen (Lukkes et al., 2017; Schiavone et al., 2009; Sun et al., 2016), suggesting a possible stress-buffering effect. Acute single ketamine treatments exerted ambiguous effects on PV expression that were unlike other enrichment protocols (O'Connor et al., 2019; Wang et al., 2014; Zhou et al., 2014), indicating that it may have a unique interaction with stress on PV neurons, likely either due to its neurochemistry or to its unique position as an acute enriching treatment.

There was little evidence of changes in mRNA or protein in the whole hippocampus (Banasr et al., 2017; Bath et al., 2016; Brenhouse & Andersen, 2011; Kim et al., 2020; Lussier & Stevens, 2016; Rossetti et al., 2018; Ueno et al., 2018) or in its subregions (Clarke et al., 2019; Krugers et al., 1996; Nowak et al., 2010; Soares et al., 2020) and the studies showing an effect reported mixed directionality (Bath et al., 2016; Kim et al., 2020; Lussier & Stevens, 2016; Riga et al., 2017; Rossetti et al., 2018; Ueno et al., 2017). The few studies including enrichment paradigms showed contradictory effects (Donato et al., 2013; Gomes da Silva et al., 2010; Kong et al., 2017; McHugh et al., 2009; Prévot & Sibille, 2020). As in the hippocampus, most evidence suggests no change in BLA PV expression after stress (Clarke et al., 2019; Gildawie et al., 2019; Lukkes et al., 2017; Santiago et al., 2018; Umemori et al., 2015).

Some other brain regions such as the whole amygdala (Lukkes et al., 2018), nucleus accumbens (Schiavone et al., 2009), and perirhinal and dorsolateral entorhinal cortices (Ueno et al., 2017)

showed evidence of the same pattern as found in the PFC: a stress-induced decrease in PV expression that could be countered by enrichment protocols. This evidence was generated by single studies, however, and elicits further inquiry for validation.

1.3.3 Sex Differences

Many studies have reported sex differences in PV cell phenotypes resulting from chronic stress. This may be due to known sexually divergent responses to stress (Altemus et al., 2014; Furman et al., 2019; Luine et al., 2017), but it also may be due to the unsuitability of chronic stress models' to assess female rodents given their ineffectiveness at eliciting depressive-like phenotypes in females compared to males (Murthy & Gould, 2018). Animal studies of PrL and IL areas of the PFC suggest that females may not show the same reductions in PV cell populations observed in males after stress. While many studies reported consistent outcomes between males and females (Leussis et al., 2012; Manzano Nieves et al., 2020; Shepard et al., 2016; Soares et al., 2020), several found stress-induced loss of PV cells (Grassi-Oliveira et al., 2016; Page & Coutellier, 2018a) and protein (do Prado et al., 2015) in males only. In one MS study, while only males showed reductions in PrL and IL PV cell numbers, both sexes performed worse on a spatial memory task compared to unstressed controls, suggesting that females may have different neurobiological adaptations to stress (Grassi-Oliveira et al., 2016). No sex differences were observed in the 3 mPFC studies that included female animals, however (Goodwill et al., 2018; Page & Coutellier, 2018a; Page et al., 2019b).

Few investigations have assessed the effects of stress or enrichment on PV cells in the HC of female animals, though these studies mostly replicate findings in males. One study found that

social isolation in juvenility and adolescence reduced the density of adult female rat PV cells in the dentate and CA2/3 areas (Harte et al., 2007), consistent with stress effects on males.

However, another MS study found increased staining for the oxidative stress marker 8-oxo-dG in dentate, CA1 and CA2/3 PV cells of juvenile females than males (Soares et al., 2020). Two MS studies of the whole HC reported no sex difference in PV cell density, immunoreactive number, or protein expression (Katahira et al., 2018; Kim et al., 2020).

The BLA was spared from a lack of animal studies on females, and two of these studies pointed toward increases in PV cells in males but not females (Gildawie et al., 2019; Guadagno et al., 2020). Females also presented more PV cells staining for the oxidative stress marker 8-oxo-dG (Soares et al., 2020), suggesting a possible mechanism for their reduced proliferation.

1.3.4 PNNs

The effects of stress on PNNs coating PV interneurons were of major interest for this review, given the influence of these structures on synaptic transmission, oxidative stress buffering capacity, and excitation/inhibition balance of the neurons they ensheath – functions that are dysregulated in key brain regions in mood disorders (Duman et al., 2016; Hare & Duman, 2020; Ng et al., 2008; Page & Coutellier, 2019a). Spijker et al. recently published a review (2020) presenting an interesting model in which animal age and stress recency modulate the effect of stress on the densities of PNNs and PV cells in the HC. Citing several studies also included in this review, they argued that animals stressed as adolescents show long-term PV cell and PNN loss (Gomes et al., 2019; Ueno et al., 2017). Animals stressed as adults, however, show an initial loss of PNNs and PV cells which recovers over several weeks to eventually reach greater

hippocampal densities of PV and PV+/PNN+ cells than before stress (Koskinen et al., 2019; Riga et al., 2017). The present systematic review finds that this pattern mostly holds up in the HC, but it remains unclear if it applies to animals stressed as pups (Murthy et al., 2019).

We did not find strong support for the stress incubation model's application to PNNs in the PFC. PNNs coating PV cells in the PrL and IL regions of the PFC were minimally affected by stress (Gildawie et al., 2019; Ueno et al., 2017; Ueno et al., 2018). One study of the mPFC presented evidence of stress in adolescence producing a delayed increase in PNN coverage of PV cells in males (Page et al., 2018b), however others found no effect (Page & Coutellier, 2018a; Pesarico et al., 2019). Fluoxetine studies likewise reported minimal effects on PNNs in the PFC (Karpova et al., 2011; Mukhopadhyay et al., 2021); a single study found a small decrease in PNNs on PV cells in the mPFC after 2 weeks of fluoxetine administration in adults (Guirado et al., 2014).

Studies of PNNs ensheathing PV cells in the HC suggest a high degree of subregion dependence, although a dearth of studies assessing all possible combinations of animal age, stress recency, stressor type, and subregion leaves many holes in our understanding. Area CA1 showed the strongest evidence for early PNN reductions (Ueno et al., 2017) and late augmentations (Koskinen et al., 2019; Riga et al., 2017), although this was not entirely consistent (Murthy et al., 2019). This pattern was not well supported in the dentate gyrus (Murthy et al., 2019), areas CA2/3 (Ueno et al., 2017), or the whole hippocampus (Gomes et al., 2019; Pesarico et al., 2019; Ueno et al., 2018). An impressive number of studies assessed the effects of fluoxetine treatment on PNNs in the HC, reporting mixed findings with the most robust evidence being a decrease in PNNs on PV cells in area CA1 (Guirado et al., 2014; Karpova et al., 2011; Mukhopadhyay et al.,

2021; Umemori et al., 2015), an effect that may not last long-term (Mukhopadhyay et al., 2021; Umemori et al., 2015). Fluoxetine given to adults appears to reduce PV cell and PNN densities in CA3 without changing the percentage of PV cells covered by PNNs (Guirado et al., 2014; Ohira et al., 2013).

Not enough information is available to grasp the effects of stress on PNNs in the BLA. For example, some studies reported single measures such as the fraction of PV cells surrounded by PNNs without complementary measures such as the overall densities of PV cells and PNNs that would elucidate whether PNNs are reduced specifically on PV cells or globally, or if PV cell numbers are increased without an accompanying increase in PNNs. Many studies reported no or mostly no effect of stressors or enrichment on PNNs coating PV cells in the region (Gildawie et al., 2019; Guadagno et al., 2020; Pesarico et al., 2019; Vazquez-Sanroman et al., 2021). One study reported that juvenile-adolescent social isolation reduced the fraction of PV cells staining for PNNs, and that stress increased the activity of PNN-coated PV cells in the region while enrichment decreased it (Vazquez-Sanroman et al., 2021). A paper by Umemori and colleagues suggests that global PNN coverage of PV cells and elsewhere was reduced by perinatal fluoxetine administration to mothers (Umemori et al., 2015). Of interest, Guadagno et al. (2020) recently reported hemisphere-dependent changes in PNNs on BLA PV cells in males but not females subjected to LB/LN.

1.3.5 Functional consequences

Stress during infancy appeared to produce opposite immediate and delayed effects on excitatory inputs to PrL PV cells. In one study, a 2-day LH protocol acutely reduced the amplitudes of

miniature excitatory postsynaptic currents (mEPSCs) on PV cells in adolescent males classified as helpless by their behavior (Perova et al., 2015). On the other hand, Wieck et al. (2013) found that MS increased the proportion of adolescents' PV cells expressing the NMDA receptor subunit NR2A. On the other hand, adolescent social isolation reduced the E/I ratio of PV cells in the dorsomedial PFC (comprising the ACC and PrL) of adult male mice (Bicks et al., 2020). Another study found no effect of maternal restraint on offspring c-Fos or NMDA subunit NR1 subunit staining in PV cells (Heslin & Coutellier, 2018) in adulthood. Altogether, these studies differ too widely in timing and type of stressor application and in the measure assessed to reconcile; in particular, changes in the expression of NMDA receptor subunits on PV neurons do not necessarily indicate electrophysiological changes to PV neurons in the same direction.

Individual studies of PV cell activity, glutamatergic input and oxidative stress markers found no effect of stressors in the IL cortex (Heslin & Coutellier, 2018; Soares et al., 2020). One study of adult rats subjected to CVS found a decrease in PV cells co-expressing glucocorticoid receptors, suggesting that PV cells may be implicated in the loss of a negative feedback loop in the HPA axis in chronic stress (McKlveen et al., 2019).

Studies of the mPFC and whole PFC found increased markers of glutamatergic input onto (Shepard et al., 2016) and activity of (Page et al., 2019b) PV cells in rodents stressed as adults, and possible sex differences in intracellular signaling with upregulated ERK activity in stressed females but not males (Shepard & Coutellier, 2017). Conversely, chronic fluoxetine administration to male adults reduced perisomatic PV and synaptophysin puncta on pyramidal neurons, suggesting reduced innervation of these cells (Guirado et al., 2014). A restraint study on adolescents found that 2 days of 6 hours' daily restraint increased PV cell dendritic spine

formation and elimination rates, whereas 7 days of restraint did not change either metric. This effect was modulated by chemogenetic inhibition and activation of PV cells before daily restraint sessions (Ng et al., 2018).

No immediate (Peric et al., 2018) or delayed (Mukhopadhyay et al., 2021) effects of stress have been reported on DG PV cell activity, but early life stress increased PV cell oxidative stress, particularly in females (Schiavone et al., 2013). In a recent study, chronic fluoxetine intake resulted in hyperpolarization and reduced firing frequency of dentate PV cells that may be due to increased potassium channel activity. This effect was eliminated by blockade or PV cell-specific knockout of the inhibitory 5HT_{5A} receptor (Sagi et al., 2020).

While recent stress increased CA1 sIPSC frequency onto pyramidal neurons in restrained adult male rats (Hu et al., 2010), Riga et al. (2017) found the opposite effect on SDPS-treated male adults 2-3 months after social defeat but with isolation up to that point. On the other hand, one study that exposed mice to a MSEW protocol found no difference in the c-Fos-positive fraction of PV cells in adults, suggesting their activity was unchanged (Murthy et al., 2019). Early life stress further increased PV cell oxidative stress markers in juveniles, particularly females (Soares et al., 2020). A single enrichment study found that acute isoflurane administration at subanesthetic levels increased FosB intensity in PV cells of adults, suggesting more activity (Antila et al., 2017). One study of the dorsal hippocampus found reduced sIPSC frequency on pyramidal neurons in adult rats subjected to SDPS, suggesting decreased PV cell activity, an effect that was eliminated by PNN digestion using chondroitinase ABC a month prior to measurement (Sagi et al., 2020).

Minimal information exists concerning the effects of stress on the generation of theta oscillations by PV neurons. To our knowledge, Hu et al. (2010) is the only report comparing theta power in PV cells of stressed animals; they found increases in relative theta power elicited by the muscarinic receptor agonist carbachol to be unchanged between stressed and unstressed adults, but that increases in theta power due to the cholecystokinin analog CCK8-S were lost in stressed rat CA1 PV neurons. The effects of stress on PV cell theta oscillations, particularly in the HC, represents a gap in our understanding of electrophysiological changes induced by adversity.

Many studies of the BLA described changes in PV cell activity (via c-Fos expression and electrophysiological parameters) that were stress recency-dependent, however they often conflicted. Stressors produced immediate increases in PV cell activity in some instances (Lukkes et al., 2012; Regev-Tsur et al., 2020; Reznikov et al., 2008) and decreased activity in another account (Guadagno et al., 2020). Similarly, delayed effects of chronic stress produced conflicting effects with some increases (Guadagno et al., 2020) and decreases (Reznikov et al., 2008) in activity, and some studies finding little to no change to balance out the lot (Ebertowska et al., 2020; Jiang et al., 2009; Lukkes et al., 2012; Varga et al., 2016). No stress-associated changes in PV cell oxidative stress markers were observed (Soares et al., 2020). One interesting study found LB/LN to reduce juveniles' PV cell innervation of both pyramidal neurons and PV cells in the region (Santiago et al., 2018), while the single enrichment study assessing BLA PV cell activity found juvenile environmental enrichment to reduce PV cell activity in adolescent females (Vazquez-Sanroman et al., 2021).

The lateral amygdala was assessed in two studies, one of which found reduced PV-c-Fos colocalization in adults stressed during the early postnatal period (Ebertowska et al., 2020) and the other which found PV-c-Fos colocalization reduced in the dorsolateral but not in the ventrolateral or ventromedial subfields of adults that were isolated during juvenility and adolescence (Lukkes et al., 2012). However, both studies subjected animals to chronic stressors followed by a rest period, then an acute stressor immediately before sacrifice, making it difficult to determine which manipulation was responsible for the outcome.

One study of the barrel cortex found that adolescent chronic restraint decreased PV cell activity and excitability, and that environmental enrichment increased activity (Chen et al., 2018).

Finally, an investigation of the nucleus accumbens shell found that PV cell excitability may have been increased by UCMS in adulthood, as measured by firing frequency in response to current injection, although resting membrane potential and action potential threshold remained unchanged (Xiao et al., 2020).

1.3.6 Human postmortem studies

In the brains of MDD patients, PV cells have been most extensively studied in the dorsolateral PFC (dlPFC), with somewhat conflicting findings (Table 5). One study found decreased PV mRNA expression (Chung et al., 2018), while others found no change in PV expression (Song et al., 2019) or cell number or density (Alcaide et al., 2019; Beasley et al., 2002; Regev-Tsur et al., 2020) in MDD compared to matched controls. Khundakar et al. (2010) found decreased PV staining intensity in the dlPFC layer VI but no such change in layers II-V. Other areas examined

in samples from MDD patients include the ACC and subgenual ACC, the HC, the OFC, and the auditory association cortex. While most studies reported no changes in PV cell density or other measures in MDD compared to controls, one found decreased PV cell density in the OFC of MDD patients (Rajkowska et al., 2007) and Tripp et al. (2012) reported reduced PV mRNA expression in the subgenual ACC in MDD.

The dlPFC/BA9 was also the most extensively studied brain region in people with BD. While PV cell number, density, and NR2A expression in PV cells were not found to be altered (Alcaide et al., 2019; Bitanirwe et al., 2010; Sakai et al., 2008), there was evidence of reduced PV mRNA expression compared with psychiatrically healthy controls reported in three studies (Chung et al., 2018; Sibille et al., 2011; Volk et al., 2016), although in Sibille et al.'s study this effect was eliminated by the exclusion of case-control pairs with potentially confounding factors. Two investigations of the amygdalar subfields in BD patients have, for the most part, reported no change in PV cell number nor density (Berretta et al., 2015; Pantazopoulos et al., 2007). The only discrepancy was in the lateral amygdalar nucleus, where Berretta and colleagues (2015) reported decreased PV cell density compared to controls, whereas the same team earlier reported no change between groups (Pantazopoulos et al., 2007). In the hippocampal subfields of BD patients, several studies have assessed PV cell number and density with some conflicting results. Findings of decreased PV cell numbers in CA1, CA2, CA4, and the parasubiculum in individual studies have been countered by findings of no change in PV cell numbers across hippocampal subregions (Chu et al., 2016; Knable et al., 2004; Pantazopoulos et al., 2010; Wang et al., 2011). The entorhinal cortex, despite one null report (Kim et al., 2020), had lower PV cell density in two studies (Pantazopoulos et al., 2010; Wang et al., 2011). Individual studies have examined

BA24 and the thalamic reticular nucleus (TRN) of BD patients and found increased clustering but unchanged density of PV cells in BA24 (Cotter et al., 2002) and decreased total PV cell number in the TRN of BD patients (Steullet et al., 2018).

Unfortunately, while many studies included the brains of people who died by suicide, cause of death was rarely a subject of analysis. In one of the few studies that did assess the effects of suicide on PV neurons, suicide was not found to associate with changes in PV mRNA in BD (Sibille et al., 2011). One study separating BD subjects into low- and non-low-GABA marker phenotypes based on their mRNA expression of GABAergic markers including PV found that low-GABA marker subjects were less likely to have died by suicide (Volk et al., 2016). This suggests that parvalbumin may be involved in the molecular signature of suicidality.

As of yet, there is little evidence of PNN changes in mood disorders in humans. Two studies have examined PFC subregions (Alcaide et al., 2019; Tanti et al., 2020). Alcaide et al. reported no changes in PNNs in the dlPFC of depressed patients, but reductions in overall PNN densities in the same region in BD. As this increase was not accompanied by a change in the density of PV cells, or in the fractions of PV cells and PNNs colocalized with one another, the reduction in PNNs was likely balanced between PV and non-PV cells. Further, individuals with a past psychotic episode, pooled from people with BD and schizophrenia, also displayed reduced dlPFC PNN density, suggesting that the loss shown in BD may pertain more to psychosis.

Subgroup analysis by Tanti et al. (2020) found PNN increases in the vmPFC of depressed suicides with a history of child abuse compared to depressed suicides and nonpsychiatric

controls with no such history. This suggests that PNNs may be lastingly increased by early-life adversity, which is a strong predictor of later depression and suicidality (Felitti et al., 1998). Further cross-sectional studies examining early life stress and neuropsychiatric disorders, and which of these phenomena more faithfully predict changes in PV cells and PNNs in humans, will be useful to elucidate the culprit in the matter.

1.4 Discussion

1.4.1 PV cell loss

Chronic stress reduced PV cell numbers in subregions of the PFC and HC and increased numbers in the BLA, with some modulation of this effect by animal age, sex, and subregion. Work by the Brenhouse and Coutellier research groups in stressed animals points to several likely interacting culprits explaining PV cell loss: systemic inflammation (Brenhouse & Andersen, 2011; Wieck et al., 2013), local neuroinflammation (Brenhouse & Andersen, 2011; Grassi-Oliveira et al., 2016), increased excitatory input onto PV cells (Ganguly et al., 2015; Shepard & Coutellier, 2017; Wieck et al., 2013), and oxidative stress in PV cells (Soares et al., 2020). It should be noted that PV cell “loss” did not necessarily directly result from PV cell death in certain brain regions but may have instead been due to reduced proliferation and maturation of PV cell precursors during postnatal development; a combination of PV cell death and impaired development may also fully explain the effect. Single-cell RNA-seq has promise to approach this question by refining our understanding of the transcriptomic signature of PV cells maturation and uncovering critical pathways affected by stress exposure in those cells.

Reductions in PV cells were matched by losses of PV mRNA and protein expression in the PFC, although these were inconsistent, and the predominant finding was null. Antidepressant treatment during stress, particularly with fluoxetine, showed some efficacy to counteract PV cell loss, suggesting that PV neurons are cellular substrates of both stress-induced depressive-like outcomes and of antidepressants' ability to buffer this phenomenon.

1.4.2 Enrichment

Enrichment effects were most consistent in hippocampal areas CA1, CA2, and CA3. Here multiple studies found that enrichment paradigms increased PV cell numbers alone or protected from stress-induced decreases in PV cell density. It should be noted that all enrichment studies in regions CA1-3 assessed adult males, except for Yang et al. (2015), which examined adolescent males.

Many other studies found enrichment to produce different effects on PV neurons when administered during a stressor than when given alone. Enrichment often played a buffering role on the impact of stress, preventing changes in PV cell phenotypes. This directionality of effect was rarely maintained when animals were exposed to enrichment in a congenial environment, however.

The type of enrichment plays a major role in its outcome as well. Fluoxetine administration, considered in this review as a form of enrichment, is the best representative example of the stress buffering effect, at times reducing numbers of PV cells and PNNs in the HC and PFC when administered on its own but typically preventing stress-induced PV cell loss in these regions. Environmental enrichment and physical exercise regimens were less potent influencers of PV

cells, and were not administered concurrently with stressors in any studies in this review (ostensibly due to logistic incompatibilities). Ketamine is in a category of its own as a fast-acting antidepressant, and its unique pharmacology seems to manifest in drastically different effects on PV cells compared to other enrichment paradigms.

1.4.3 Sex-specific findings

Milner et al.'s report (2013) regarding the effect of the estrus cycle on the stress responses and μ -opioid receptor distribution in hilus PV cell dendrites illustrates a further layer of complexity to the study of stress in female animals. The finding of estrus cycle effects on PV neurons represents a field of study that may prove fruitful for understanding ovulation cycle-related changes in stress sensitivity in humans (Olson et al., 2015; Ossewaarde et al., 2013).

While findings in the HC were similar in males and females, reductions in PV cells in the PFC and increases in the BLA were less consistent in female animals. The study of Soares and colleagues (2020) suggests that juvenile females exhibit more oxidative stress in PV cells after MS than males in the HC and BLA, however it is unclear if this translates to changes in cell numbers or activity, further complicating the question of sex differences.

The preponderance of animal studies showing effects in males calls into question the suitability of current stress paradigms as models of conditions that are more frequent in women. Hopefully, recently developed social stress paradigms adapted for female rodents will provide improved opportunities to study sex-specific neurobiological responses to psychosocial stress (Furman et al., 2019; Takahashi et al., 2017). Further, the recent two-hit model which produced greater

phenotypic changes than maternal separation alone in females shows promise as an improved model for interrogating sex-specific neurobiological responses to stress (Gildawie et al., 2021).

1.4.4 Why are PV neurons impacted by stress?

It would seem that due to their fast-spiking electrophysiology and their critical role in gating pyramidal neuron output, PV neurons are particularly sensitive cells, more vulnerable to oxidative stress and excitotoxicity than many other neuronal populations (Cabungcal et al., 2013; Moga et al., 2002). In conditions of chronic stress, involving elevated inflammation in the local microenvironment and oxidative stress within neurons, some PV interneurons are likely lost due to atrophy and apoptosis or mature incompletely during postnatal neurodevelopment. Further, given their downregulation of GRs in the infralimbic cortex following stress (McKlveen et al., 2016), they are likely implicated in the HPA axis dysregulation found in chronic stress conditions. The crucial roles played by PV cells in microcircuits and gating of excitatory projections may make their casualties felt widely in the brain, as evidenced by the many animal studies in this review that found correlations between behavioral changes and altered PV cell phenotypes after stress.

1.4.5 Impact of stress severity and duration on PV neurons

Recent chronic stress studies aimed at studying animal models of mood disorders, such as Spijker group's SDPS model (Koskinen et al., 2019; Riga et al., 2017) and Brenhouse group's recent "two-hit" adversity model involving MS followed by SI (Gildawie et al., 2021), have increased the intensity and/or duration of the stress paradigm. These models have been largely successful at eliciting more pronounced behavioral phenotypes than previously established

paradigms. In particular, the two-hit model produced greater effects in females than simple MS, suggesting it to be a viable alternative to other stress models that do not produce changes in female animals as reliably as in males.

1.4.6 Functional changes

The functional changes to PV neurons observed in chronic stress states underscore the likely implication of these interneurons in dysregulated executive function, memory, learning, and emotions commonly found in mood disorders. In this review, we found a wealth of evidence suggesting changes to PV cell E/I balance and other electrophysiological parameters, but often in opposite directions. We are unable to reconcile these disparate findings, and the early hyperexcitability-late hypofunction model proposed by Spijker et al. (2020) was not entirely supported by the reviewed literature. These findings are far from depicting the full picture, which would require a more detailed understanding of how PV cells interact with other neurons and glia, and how such interactions are affected by stress. Direct replications of several studies included in this review assessing functional outcomes in key brain regions such as the PFC and BLA with manipulations of pertinent variables such as age, sex, and stress recency will be useful to confirm robust effects, and novel experiments that assess neglected factors such as animal species/strain and stressor type and intensity may be promising ventures to elucidate the determinants of observed PV cell changes.

1.4.7 PNNs and stress incubation

The impact of psychopathology and stress on PNNs was included in this review as they seem to influence every aspect of PV neuron physiology and connectivity. The effect of PNN

degradation on PV cells is rather hard to decipher, however, as this depends on the connectivity of PV cells with principal cells, but also their interconnectivity with other inhibitory neurons, is network/region-dependent, and affects a variety of electrophysiological properties. Degrading PNNs through enzymatic digestion or selective KD/KO of some of their components have been shown to decrease PV cells firing rate, increase their spiking variability, modifies their resting membrane potential and input resistance, their excitability, perhaps through changes in both excitatory and inhibitory inputs onto PV cells (Carceller et al., 2020; Christensen et al., 2021) (see review by Wingert & Sorg (2021) for an in-depth description of the diverse functions of PNNs). Some of those changes are likely to participate in the overall decreased inhibitory drive onto principal cells observed following PNN removal and increased firing of pyramidal neurons (Carceller et al., 2020), but also changes in gamma and theta oscillations (Lensjø et al., 2017). According to Spijker et al.'s recent review (2020), animals stressed as adolescents show long-term PV cell and PNN loss (Gomes et al., 2019; Ueno et al., 2017). Animals stressed as adults, however, show an initial loss of PNNs and PV cells which recovers over several weeks to eventually reach greater hippocampal PV and PV+/PNN+ cell densities than before stress (Koskinen et al., 2019; Riga et al., 2017). These stress recency-dependent changes may serve as an adaptive response to adversity; in the immediate period after the traumatic event, an individual must adapt to novel threats, and PNNs are digested to promote plasticity and learning. After a prolonged period, however, chronic stress takes its toll (ostensibly in the form of neuroinflammation and oxidative stress in the cellular microenvironment); PNN production is increased and PV cells fire less frequently to prevent their own excitotoxicity. There is strong evidence for this pattern in hippocampal area CA1, but it requires validation in the rest of the HC and the PFC as well as further study of its application to female animals as the strongest

evidence comes from studies involving male animals only (Koskinen et al., 2019; Riga et al., 2017). Interestingly, studies using fluoxetine reported a similar pattern in CA1, with reductions in PNNs after recent drug administration (Guirado et al., 2014; Karpova et al., 2011; Mukhopadhyay et al., 2021; Umemori et al., 2015) that may disappear long-term (Mukhopadhyay et al., 2021; Umemori et al., 2015). The stress incubation model of PNN changes would be best assessed by experiments involving animals exposed to a variety of stressors at a variety of ages, along with different stressor “incubation” times. Antidepressant administration during stress is also worthy of exploration as a potential buffer of this phenomenon.

We recommend that future studies assessing PNNs report all relevant metrics to make any potentially important information available to other researchers. The numbers of cells staining positively for PV and/or PNNs, the proportions of the former expressing the latter and vice versa, and the staining intensities of each antigen are examples of important information that can be used to glean insight into PV cell and PNN function. Gildawie et al. 2019 and 2021 are examples of such papers with optimal data presentation.

1.4.8 Human brains: postmortem studies

Postmortem studies of brain samples from individuals with mood disorders have revealed replicated PV cell alterations in BD and MDD, although with less consistency for the latter. Our overview suggests that individuals with BD have lower PV mRNA expression in the dlPFC (a region absent in rodents; see the review by Laubach et al. (2018) on anatomical species differences) and reduced PV cell numbers in the entorhinal cortex. Although inconsistent,

evidence of decreased numbers of PV cells in hippocampal subfields of BD patients (Knable et al., 2004; Konradi et al., 2011) was somewhat comparable to findings generated in stressed animals.

The association of other brain disorders such as schizophrenia (Kaar et al., 2019) and autism (Lauber et al., 2018) with changes in PV neuron function may reflect the involvement of shared emotional and/or cognitive processing impairments among these disorders. Further research linking PV neurons to changes along these dimensions may help illuminate the links between brain disorders and inform the enduring debate over the validity of diagnoses.

The limited translatability of animal studies to human postmortem findings may be explained in part by differences in study design; animal studies mostly compared stressed to non-stressed groups rather than grouping by behavior, whereas humans were grouped into phenotypic classes (psychiatric diagnoses), which inherently vary due to the important heterogeneity in the clinical features of these disorders. Recent postmortem findings from Tanti et al. suggest that refining the phenotypic characterization of human subjects by taking into account histories of life (such as early-life adversity) may yield more faithful neurobiological underpinnings. A thorough assessment of child abuse and/or trauma histories will thus be an important consideration for future postmortem studies, as it may be mediating the observed association between mood disorders and PV interneuron changes. Subgroup analysis for other criteria such as suicide or research domain-based criteria (e.g. anhedonia, fatigue) may also elucidate the relationship of PV cells to mood and behavior in humans. For instance, Bath's group has linked PV cell loss in the OFC with poorer cognitive performance in female mice (Goodwill et al., 2018), a finding that

could echo the reduced density of PV cells in the same region of MDD subjects found in a postmortem study (Rajkowska et al., 2007) since cognitive impairments are often associated with MDD. Refining phenotypic characterizations of subjects beyond diagnosis is therefore crucial, but often impossible in postmortem studies, which limits our ability to confront these observations with animal studies.

It is important to highlight the increasing evidence suggesting that there are likely several classes of PV interneurons. Donato et al. (2013) first reported that PV expression in rodent PV cells correlates with their GABA production and found enrichment effects specifically on high-PV-expressing cells. Riga et al. (2017) continued this line of inquiry and described a loss of low-PV cells and a reciprocal increase in high-PV cells in the CA1 stratum pyramidale after SDPS.

Advances in postmortem brain research have recently allowed for the description of PV interneuron subtypes in humans (Nagy et al., 2020). In this study, single-nucleus RNA-seq of dIPFC samples identified two subpopulations differentiated by high and low expression of GABAergic markers, and comparison of samples from depressed-suicides and matched controls revealed a more robust downregulation of genes in the low-GABA cell population in cases.

Whether these PV cell subtypes identified in rodent HC and human PFC are of the same nature remains to be determined. Further studies assessing the expression of orthologs in the same brain regions, as well as electrophysiological correlates of the subtypes, may be useful to elucidate the relationship and identities of PV interneuron classes. Aside from identifying latent neuronal subpopulations, future postmortem studies combining single-nucleus sequencing with validation approaches such as quantitative in situ hybridization should help to determine the molecular

signatures of PV cells in mood disorders as well as potential changes in the way these neurons interact with other cell types.

1.4.9 Study Limitations

This study did not assess the possibility of different stress models exerting unique effects on PV cell outcomes, which is highly likely given their differing degrees of construct validity as mood disorder models. With the weight of literature currently available on PV neurons in chronic stress, such an analysis is feasible but would be weak due to the effects of other confounding variables such as animals' age, sex, and stress recency. Another limitation of this review is that it did not assess the effect of a stressor "dose" on PV cells, e.g., comparing different durations of an identical stressor. Again, such an analysis would have very low power; thus, it was omitted in order to limit this review's scope. Furthermore, rats and mice alike (as well as individual studies with degus (Helmeke et al., 2008) and tree shrews (Czeh et al., 2005)) were grouped together for analysis and any possible differences between species or strains were ignored, again for the purpose of limiting study scope. Future studies should take these considerations into account and direct comparisons of stress models, stress doses, and species will be useful to elucidate their respective influences on outcomes of interest.

1.5 Concluding Remarks

Despite a largely inconsistent literature, mood disorders and chronic stress in rodents were found to affect PV interneurons most frequently in the PFC, HC, and BLA. The impact of stress on PV interneurons and PNNs in humans is sorely lacking compared to rodents and represents a potentially fruitful avenue of future research. In animals, enrichment paradigms showed some

evidence of buffering stress effects on PV interneurons, particularly in the HC. Interestingly, it appears that different enrichment types exert unique effects on PV cells, and that these may be region- and age-specific. Finally, sex differences in both PV cell alterations and stress responsiveness were evident and will also require further study.

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Table 1: PV neuron alterations in the prefrontal cortex of stressed animals

Species	Age during manipulation	Age at measurement	Sex	Experimental Paradigm	Brain Region	Method	Measure	Outcome	Reference
Mouse (C57/BL6)	Adolescent	Adolescent	♂	RS 6h/day 21 days	Prelimbic cortex	IHC	Total PV cell number; PV cellular intensity	no change	[27] Clarke et al. (2018)
Rat (Wistar)	Adolescent-adult	Adult	♂	CMS 9 weeks	Prelimbic cortex	IHC	Total PV cell number	no change	[32] Czeh et al. (2018)
Mouse (C57/BL6)	Adult	Adult	♂	RS 1h/day for 14 days; sacrifice immediately or 1 month later	Prelimbic cortex	IHC	Total PV cell number	no change	[45] Friedman et al. (2017)
Rat (Sprague-Dawley)	Early postnatal	Adolescent	♂	MS 4h/day	Prelimbic cortex	IHC	PV cell density	decreased	[48] Ganguly et al. (2015)
Rat (Sprague-Dawley)	Early postnatal	Juvenile; adolescent; adult	♂♀	MS 4h/day; 0, 20, or 50 days rest	Prelimbic cortex	IHC and WFA stain	PV+/PNN+ cell density; PV cell density; PV+ PNN intensity; PNN+ PV intensity; PV intensity	increased PV+ PNN intensity at P70 in males; no change in others	[51] Gildawie et al. (2019)
Rat (Sprague-Dawley)	Early postnatal-adolescent	Adult	♂♀	MS 4h/day; SI or pair housing from P21-P35	Prelimbic cortex	IHC and WFA stain	PV cell number; PV intensity; PNN number; PNN intensity; PV+/PNN+ cell number; PNN+ fraction of PV cells; PNN+ PV intensity; PV+ PNN intensity	PV cell number and PNN+ fraction of PV cells reduced in females by MS+SI compared to SI alone; PNN intensity reduced by MS+SI in females compared to MS or SI alone; PV+ PNN intensity reduced by MS+SI in females compared to MS alone	[52] Gildawie et al. (2021)
Rat (Sprague-Dawley)	Early postnatal	Adolescent	♂♀	MS 4h/day	Prelimbic cortex	IHC	Total PV cell number	decreased in males, no change in females	[59] Grassi-Oliviera et al. (2016)
Degu	Early postnatal	Juvenile	♂	MS 3x1h/day	Prelimbic cortex	IHC	PV cell density	no change	[65] Helmeke et al. (2008)

Degu	Early postnatal	Adolescent	♂	MS 3x1h/day	Prelimbic cortex	IHC	PV cell density	no change	[65] Helmeke et al. (2008)
Npas4 HET and wild-type mice	-	Adult	♂	Maternal RS (GD7-19) 30 mins twice per day	Prelimbic cortex	IHC	Total PV cell number; total PV+/c-Fos+ cell number; average NR1 puncta per PV cell	no change	[66] Heslin and Coutellier (2018)
Rat (Sprague-Dawley)	Early postnatal	Adolescent; adult	♂	MS 4h/day	Prelimbic cortex	IHC	PV cell density	decreased at P40, no change at P100	[92] Leussis et al. (2012)
Mouse (C57/BL6)	Early postnatal	Early postnatal; juvenile; adolescent; adult	♂♀	LB/LN 7 days	Prelimbic Cortex	IHC	PV cell density	increased in adults	[101] Manzano Nieves et al. (2020)
Rat (Sprague-Dawley)	Early postnatal	Adult	♂	MS 2x3h/day	Prelimbic cortex	IHC	PV cell density	no change	[125] Ohta et al. (2019)
Mouse (C57/BL6)	Adolescent	Adolescent; adult	♂♀	UCMS 2 weeks; 6 or 40 days rest before sacrifice	Prelimbic cortex	IHC	Total PV cell number	decreased in males	[129] Page and Coutellier (2018a)
Mouse (C57/BL6)	Adult	Adult	♂♀	UCMS 4 weeks	Prelimbic cortex	IHC	Total PV cell number	increased	[154] Shepard et al. (2016)
Rat (Sprague-Dawley)	Early postnatal	Juvenile	♂♀	MS 4h/day 19 days	Prelimbic Cortex	IHC	8-oxo-dG+ fraction of PV cells; PV+ cell 8-oxo-dG intensity; PV cell number; PV intensity	increased 8-oxo-dG+ fraction; PV intensity higher in females than males	[156] Soares et al. (2020)
Mouse (C57/BL6)	Juvenile-adolescent	Adolescent	♂	SI 5 weeks	Prelimbic cortex layers 2/3 and L5/6	IHC and WFA stain	PV cell density; PNN+ fraction of PV cells; PV fluorescence intensity; PV soma area	decreased PV soma area	[169] Ueno et al. (2017)
Mouse (C57/BL6)	Juvenile; adult	Adolescent; adult	♂	CUS 7 days	Prelimbic cortex	IHC and WFA stain	PV cell density; PNN+ fraction of PV cells; PV+ fraction of PNNs; PV fluorescence; PV soma area	no change	[170] Ueno et al. (2018)

Mouse (C57/BL6)	Adolescent-adult	Adult	♂	CSIS 7 weeks. After stress, mice housed individually for 1 year	Prelimbic cortex	IHC	PV cell density	decreased	[178] Wang et al. (2019)
Rat (Sprague-Dawley)	Early postnatal	Juvenile	♂	MS 4h/day	Prelimbic cortex	IHC; Western blot	PV cell density; PV protein content	no change	[19] Brenhouse and Andersen (2011)
Rat (Sprague-Dawley)	Early postnatal	Adolescent	♂	MS 4h/day	Prelimbic cortex	IHC; Western blot	PV cell density; PV protein content	decreased protein and density	[19] Brenhouse and Andersen (2011)
Rat (Sprague-Dawley)	Early postnatal	Adolescent	♂♀	MS 4h/day	Prelimbic cortex	Western blot	PV protein content	decreased in males	[34] do Prado et al. (2015)
Rat (Sprague-Dawley)	Early postnatal	Adolescent; adult	♂♀	MS 4h/day	Prelimbic cortex	Western blot	PV protein content	decreased at P40, no change at P100	[92] Leussis et al. (2012)
Rat (Sprague-Dawley)	Adult	Adult	♂♀	RS 3h/day for 10 days	Prelimbic cortex	qPCR	PV mRNA expression	no change	[112] Moench et al. (2020)
Rat (Sprague-Dawley)	Adult	Adult	♂♀	Acute elevated platform stress	Prelimbic cortex	qPCR	PV mRNA expression	no change	[112] Moench et al. (2020)
Rat (Sprague-Dawley)	Adult	Adult	♂♀	RS 3h/day for 10 days; elevated platform stress on day 11	Prelimbic cortex	qPCR	PV mRNA expression	no change	[112] Moench et al. (2020)
Rat (Sprague-Dawley)	Adult	Adult	♂♀	RS 3h/day for 10 days; 7 days rest	Prelimbic cortex	qPCR	PV mRNA expression	increased	[112] Moench et al. (2020)
Rat (Sprague-Dawley)	Adult	Adult	♂♀	RS 3h/day for 10 days; elevated platform stress on day 17	Prelimbic cortex	qPCR	PV mRNA expression	increased in males	[112] Moench et al. (2020)
PV-Cre Mouse (C57/BL6)	Adolescent	Adolescent	♂	LH 1h for 2 days; mice classified as helpless or resilient	Prelimbic cortex	Electrophysiology	mEPSC and mIPSC amplitude and frequency onto PV cells	decreased mEPSC amplitude in helpless, no change in others	[136] Perova et al. (2015)

Mouse (C57/BL6)	Adolescent	Adolescent	♂	RS 6h/day 3 weeks	Infralimbic cortex	IHC	Total PV cell number; PV cellular intensity	no change	[27] Clarke et al. (2018)
Rat (Wistar)	Adolescent-adult	Adult	♂	CMS 9 weeks	Infralimbic cortex	IHC	Total PV cell number	decreased in anhedonic but not resilient rats	[32] Czeh et al. (2018)
Rat (Sprague-Dawley)	Early postnatal	Adolescent	♂	MS 4h/day	Infralimbic cortex	IHC	PV cell density	decreased	[48] Ganguly et al. (2015)
Rat (Sprague-Dawley)	Early postnatal	Juvenile; adolescent; adult	♂♀	MS 4h/day; 0, 20, or 50 days rest	Infralimbic cortex	IHC and WFA stain	PV+/PNN+ cell density; PV cell density; PV+ PNN intensity; PNN+ PV intensity; PV intensity	no change	[51] Gildawie et al. (2019)
Rat (Sprague-Dawley)	Early postnatal-adolescent	Adult	♂♀	MS 4h/day; SI or pair housing from P21-P35	Infralimbic cortex	IHC and WFA stain	PV cell number; PV intensity; PNN number; PNN intensity; PV+/PNN+ cell number; PNN+ fraction of PV cells; PNN+ PV intensity; PV+ PNN intensity	PNN intensity and PV+ PNN intensity reduced in females by MS+SI compared to MS or SI alone	[52] Gildawie et al. (2021)
Rat (Sprague-Dawley)	Early postnatal	Adolescent	♂♀	MS 4h/day	Infralimbic cortex	IHC	Total PV cell number	decreased in males	[59] Grassi-Oliviera et al. (2016)
Degu	Early postnatal	Juvenile	♂	MS 3x1h/day	Infralimbic cortex	IHC	PV cell density	no change	[65] Helmeke et al. (2008)
Degu	Early postnatal	Adolescent	♂	MS 3x1h/day	Infralimbic cortex	IHC	PV cell density	no change	[65] Helmeke et al. (2008)
Npas4 HET and wild-type mice	-	Adult	♂	Maternal RS (GD7-19) 30 mins twice per day	Infralimbic cortex	IHC	Total PV cell number; total PV+/c-Fos+ cell number; average NR1 puncta per PV cell	decreased PV cell number and PV+/c-Fos+ cell number in heterozygotes vs wild type; no change due to stress	[66] Heslin and Coutellier (2018)
Mouse (C57/BL6)	Early postnatal	Early postnatal; juvenile; adolescent; adult	♂♀	LB/LN 7 days	Infralimbic cortex	IHC	PV cell density	no change	[101] Manzano Nieves et al. (2020)

Rat (Sprague-Dawley)	Adolescent-adult	Adult	♂	CVS 14 days	Infralimbic cortex	IHC	PV+/Glucocorticoid receptor+ number	decreased	[105] McKlveen (2016)
Rat (Sprague-Dawley)	Early postnatal	Adult	♂	MS 2x3h/day	Infralimbic cortex	IHC	PV cell density	decreased	[125] Ohta et al. (2019)
Mouse (C57/BL6)	Adolescent	Adolescent; adult	♂♀	UCMS 2 weeks; 6 or 40 days rest before sacrifice	Infralimbic cortex	IHC	Total PV cell number	no change	[129] Page and Coutellier (2018a)
Mouse (C57/BL6)	Adult	Adult	♂♀	UCMS 4 weeks	Infralimbic cortex	IHC	Total PV cell number	increased in females	[154] Shepard et al. (2016)
Rat (Sprague-Dawley)	Early postnatal	Juvenile	♂♀	MS 4h/day 19 days	Infralimbic Cortex	IHC	8-oxo-dG+ fraction of PV cells; PV+ cell 8-oxo-dG intensity; PV cell number; PV intensity	no change	[158] Soares et al. (2020)
Mouse (C57/BL6)	Juvenile-adolescent	Adolescent	♂	SI 5 weeks	Infralimbic cortex layers 2/3 and L5/6	IHC and WFA stain	PV cell density; PNN+ fraction of PV cells; PV fluorescence intensity; PV soma area	no change	[169] Ueno et al. (2017)
Mouse (C57/BL6)	Juvenile; adult	Adolescent; adult	♂	CUS 7 days starting at P21 or P71	Infralimbic cortex	IHC and WFA stain	PV cell density; PNN+ fraction of PV cells; PV+ fraction of PNNs; PV fluorescence; PV soma area	no change	[170] Ueno et al. (2018)
Mouse (C57/BL6)	Adolescent-adult	Adult	♂	CSIS 7 weeks. After stress, mice housed individually for 1 year	Infralimbic cortex	IHC	PV cell density	decreased	[178] Wang et al. (2019)
Rat (Sprague-Dawley)	Early postnatal	Adolescent	♂♀	MS 4h/day	Infralimbic cortex	Western blot	PV protein content	decreased in males	[34] do Prado et al. (2015)
Rat (Wistar)	Adolescent-adult	Adult	♂	CMS 9 weeks	Anterior Cingulate cortex	IHC	Total PV cell number	no change	[32] Czeh et al. (2018)
Degu	Early postnatal	Juvenile	♂	MS 3x1h/day	Anterior Cingulate cortex	IHC	PV cell density	no change	[65] Helmeke et al. (2008)

Degu	Early postnatal	Adolescent	♂	MS 3x1h/day	Anterior Cingulate cortex	IHC	PV cell density	increased	[65] Helmeke et al. (2008)
Mouse (C57/BL6)	Juvenile-adolescent	Adolescent	♂	SI 5 weeks	Dorsal Anterior Cingulate cortex layers 2/3 and L5/6	IHC and WFA stain	PV cell density; PNN+ fraction of PV cells; PV fluorescence intensity; PV soma area	decreased layer 2/3 PNN+ fraction of PV cells and PV fluorescence intensity	[169] Ueno et al. (2017)
Mouse (C57/BL6)	Juvenile; adult	Adolescent, adult	♂	CUS 7 days starting at P21 or P71	Dorsal Anterior Cingulate cortex	IHC and WFA stain	PV cell density; PNN+ fraction of PV cells; PV+ fraction of PNNs; PV fluorescence; PV soma area	no change	[170] Ueno et al. (2018)
Mouse (C57/BL6)	Adolescent-adult	Adult	♂	CSIS 7 weeks. After stress, mice housed individually for 1 year	Anterior Cingulate cortex	IHC	PV cell density	decreased	[178] Wang et al. (2019)
Degu	Early postnatal	Juvenile	♂	MS 3x1h/day	Precentral Medial cortex	IHC	PV cell density	no change	[65] Helmeke et al. (2008)
Degu	Early postnatal	Adolescent	♂	MS 3x1h/day	Precentral Medial cortex	IHC	PV cell density	increased	[65] Helmeke et al. (2008)
Mouse (C57/BL6)	Juvenile-adolescent	Adult	♂	SI P21-35, group housing until measurement at P60-65	Dorsomedial PFC (including prelimbic and anterior cingulate regions)	Electrophysiology	200 pA-elicited spike frequency; sIPSC frequency	reduced (both)	[12] Bicks et al. [2020]
Mouse (C57/BL6)	Adult	Adult	♂♀	UCMS 4 weeks	Medial Prefrontal cortex	IHC	Total PV+/c-Fos+ cell number	increased	[132] Page et al. (2019b)
Npas4 HET and wild-type mice	Adolescent	Adult	♂	CMS 2 weeks; 4 weeks rest	Medial Prefrontal cortex	IHC and WFA stain	Total PV cell number; PNN+ fraction of PV cells	increased PNN+ fraction in wild-type mice	[130] Page et al. (2018b)

Rat (Sprague-Dawley)	Adult	Adult	♂	RS 6h/day for 10 days	Medial Prefrontal cortex	IHC and WFA stain	Total PV cell number; Total PNN+/PV+ cell number	increased total PV cell number	[137] Pesarico et al. (2019)
GAD67(+/-GFP) (HET) mice	-	Juvenile	♂	Maternal RS: 45 mins 3x/day from GD15 to GD17.5; BrdU injection IP once at GD12 or GD15	Medial Prefrontal Cortex	IHC	PV+/-GFP+ cell density	decreased	[168] Uchida et al. (2014)
GAD67(+/-GFP) (HET) mice (C57/BL6)	-	Juvenile	♂	Maternal RS: 3x45mins/day under halogen light during day from GD15-GD17.5; newborns given to surrogate mothers on P0	Medial Prefrontal cortex	IHC and WFA stain	Densities of PV cells, PNN+ PV cells, PNN- PV cells, Aggreca+/PV+ cells, Aggreca- PV cells; WFA intensity of PV cells; Aggreca intensity of PV cells	Decreased densities; no change in intensities	[179] Wang et al. (2018)
Mouse (C57/BL6)	-	Juvenile	♂	Maternal RS: 3x45mins/day under halogen light during day from GD15-GD17.5; newborns given to surrogate mothers on P0	Medial Prefrontal cortex	IHC and WFA stain	Densities of PV cells, PNN+ PV cells, PNN- PV cells, Aggreca+/PV+ cells, Aggreca- PV cells; WFA intensity of PV cells; Aggreca intensity of PV cells	no change	[179] Wang et al. (2018)
Mouse (C57/BL6)	Early postnatal	Adult	♂♀	LB/LN	Medial Prefrontal cortex	qPCR	PV mRNA expression	no change	[58] Goodwill et al. (2018)
GAD67(+/-GFP) (HET) mice (CD1)	-	Juvenile, adult	♂	Maternal RS: beginning on GD12, 45 mins 3x/day during daylight under bright lights	Medial Prefrontal Cortex	IHC	PV+ fraction of GAD67:GFP+ cells	decreased at P24, increased at P150	[99] Lussier and Stevens (2016)
GAD67(+/-GFP) (HET) mice (CD1)	-	Juvenile, adult	♂	Maternal RS: beginning on GD12, 45 mins 3x/day during daylight under bright lights	Medial Prefrontal Cortex	qPCR	PV:GAD1 mRNA ratio	no change at P24, decreased at P150	[99] Lussier and Stevens (2016)
Rat (Wistar)	Adult	Adult	♂	CUS 16 days or CMS 8 weeks	Medial Prefrontal cortex	IHC	PV numerical density, relative PV optical density	no change	[186] Zadrozna et al. (2011)

Mouse (C57/BL6)	Adolescent	Adolescent, adult	♂♀	UCMS 2 weeks; 6 or 40 days rest before sacrifice	Medial Prefrontal cortex	IHC and WFA stain	PNN+ fraction of PV cells	no change	[130] Page et al. (2018b)
Mouse (C57/BL6)	Juvenile	Adult	♂	2 weeks SI	Medial Prefrontal Cortex	Electrophysiology	sIPSC frequency and amplitude on PH and non-PH layer 5 pyramidal neurons	increased frequency in PH pyramidal neurons	[184] Yamamuro et al. (2020)
Mouse (C57/BL6)	Adolescent	Adult	♂	2 weeks SI	Medial Prefrontal Cortex	Electrophysiology	sIPSC frequency and amplitude on PH and non-PH layer 5 pyramidal neurons	no change	[184] Yamamuro et al. (2020)
Rat (Wistar)	Juvenile-adolescent; juvenile-adult	Adolescent, adult	♂	SI 2, 4, or 7 weeks	Prefrontal cortex	IHC	PV cell density	decreased at 4 and 7 weeks' SI but not 2	[151] Schiavone et al. (2012)
Npas4 HET and wild-type mice	Adolescent	Adult	♂	CMS 2 weeks; 4 weeks rest	Ventral Prefrontal cortex (infralimbic and dorsal peduncular cortices)	IHC and WFA stain	Total PV cell number; PNN+ fraction of PV cells	increased PNN+ fraction in wild-type mice	[130] Page et al. (2018b)
Npas4 HET and wild-type mice	Adolescent	Adult	♂	CMS 2 weeks; 4 weeks rest	Dorsal Prefrontal cortex (anterior cingulate and prelimbic cortices)	IHC and WFA stain	Total PV cell number; PNN+ fraction of PV cells	no change	[130] Page et al. (2018b)
Mouse (BALB/c)	Adult	Adult	♂♀	UCMS 2 weeks	Prefrontal cortex	qPCR; IHC	PV mRNA expression; Total PV cell number; PV+/pERK+ cell number; VGlut1 puncta number per PV cell	Increased PV mRNA, PV cell number, and PV+/pERK+ cell number in females but not males. Increased VGlut1 puncta/PV cell in males and females	[155] Shepard and Coutellier (2017)
Mouse (BALB/c)	Adult	Adult	♂♀	UCMS 4 weeks	Prefrontal cortex	qPCR; IHC	PV mRNA expression; Total PV cell number; VGlut1 puncta number per PV cell	Increased VGlut1 puncta/PV cell in females	[155] Shepard and Coutellier (2017)

Mouse (C57/BL6)	Early postnatal	Early postnatal, juvenile	♀	LB/LN	Prefrontal cortex	qPCR	PV mRNA expression	decreased at P21	[58] Goodwill et al. (2018)
Npas4 HET and wild-type mice	-	Adult	♂♀	Maternal RS (GD7-19) 30 mins 2x/day	Prefrontal cortex	qPCR	PV mRNA expression	increased in heterozygotes vs wild type in males but not females; no change due to stress	[66] Heslin and Coutellier (2018)
Rat (Wistar)	Adult	Adult	♂	CMS 7 weeks	Prefrontal cortex	qPCR	PV mRNA expression	no change	[144] Rossetti et al. (2018)
Mouse (C57/BL6)	Adult	Adult	♂♀	UCMS 2 or 4 weeks	Prefrontal cortex	qPCR	PV mRNA expression	increased in females but not males	[154] Shepard et al. (2016)
Rat (Sprague-Dawley)	Adult	Adult	♂	CUS 36 days	Prefrontal cortex	Western blot	PV protein content	no change	[6] Banasr et al. (2017)
Rat (Sprague-Dawley)	Early postnatal	Juvenile, adolescent	♂♀	MS 4h/day	Prefrontal cortex	Western blot	PV protein content	decreased in female juveniles and male adolescents	[67] Holl et al. (2014)
Rat (Sprague-Dawley)	Early postnatal; adolescent	Adolescent	♀	MS 4h/day; LH task P41	Prefrontal cortex	Western blot	PV protein content	decreased	[96] Lukkes et al. (2017)
Rat (Sprague-Dawley)	Early postnatal; adolescent	Adolescent	♀	MS 4h/day; LH task P41; allowed to witness another rat in task 1 day before they did it.	Prefrontal cortex	Western blot	PV protein content	no change	[96] Lukkes et al. (2017)
Rat (Sprague-Dawley)	Early postnatal; adolescent	Adolescent	♀	MS 4h/day; LH tests P40-41 then sacrifice	Prefrontal cortex	Western blot	PV protein content	decreased in anhedonic MS vs non-anhedonic MS rats	[97] Lukkes et al. (2018)
Rat (Sprague-Dawley)	Juvenile-adolescent	Adolescent	♀	SI 3 weeks	Prefrontal cortex	Western blot	PV protein content	no change	[97] Lukkes et al. (2018)
Ncf1 DA allele rats (low ROS production), and Ncf1 E3 rats (high ROS production)	Juvenile-adult	Adult	♂	SI 7 weeks	Prefrontal cortex	Western blot	PV protein content	decreased by SI in E3 but not DA rats	[151] Schiavone et al. (2012)
Mouse (C57/BL6)	Adolescent	Adolescent	♂♀	RS 6h/day for 2 or 7 days	Frontal Association	Microscopy	PV cell dendritic spine formation and elimination rate	increased formation and elimination at 2 days	[119] Ng et al. (2018)

					cortex layers 2/3				
PV-Cre;Ai9-tdTomato mice (C57/BL6)	Adolescent	Adolescent	♂♀	CNO injection then RS 6h/day for 2 or 7 days	Frontal Association cortex layers 2/3	DREADD activation of PV cells; Microscopy	PV cell dendritic spine formation and elimination rate	decreased elimination at days 2 and 7	[119] Ng et al. (2018)
PV-Cre;Ai9-tdTomato mice (C57/BL6)	Adolescent	Adolescent	♂♀	CNO injection then RS 6h/day for 2 or 7 days	Frontal Association cortex layers 2/3	DREADD inhibition of PV cells; Microscopy	PV cell dendritic spine formation and elimination rate	increased formation at day 2	[119] Ng et al. (2018)
PV-Cre;Ai9-tdTomato mice (C57/BL6)	Adolescent	Adolescent	♂♀	CNO injection then RS 6h for 2 or 7 days	Frontal Association cortex layers 2/3	DREADD activation of PV cells; Microscopy	PV cell dendritic mushroom, stubby, and thin spine elimination rate	decreased mushroom spine elimination at days 2 and 7 vs RS alone	[119] Ng et al. (2018)
PV-Cre;Ai9-tdTomato mice (C57/BL6)	Adolescent	Adolescent	♂♀	CNO injection then RS 6h for 2 or 7 days	Frontal Association cortex layers 2/3	DREADD inhibition of PV cells; Microscopy	PV cell dendritic mushroom, stubby, and thin spine elimination rate	no change vs RS alone	[119] Ng et al. (2018)

Mouse and rat life stages were defined as follows: early postnatal: P0-19 (postnatal day 0-19, where day of birth is P0; juvenile: P20-30; adolescent: P31-60; and adult: P61+. Degus were examined at P45 and P90, which were termed juveniles and adolescents, respectively according to information from Colby 2012. Abbreviations: BrdU: bromodeoxyuridine; CMS: chronic mild stress; CSIS: chronic social instability stress; CUS: chronic unpredictable stress; GAD1/GAD67: glutamate decarboxylase; GD#: gestational day, where day of fertilization is GD0; HET: heterozygous; IHC: immunohistochemistry; IP: intraperitoneal; LB/LN: limited bedding/limited nesting; LH: learned helplessness; MS: maternal separation; PH: prominent lh (defined in paper); qPCR: quantitative polymerase chain reaction; RS: restraint stress; SI: social isolation; UCMS: unpredictable chronic mild stress; WFA: Wisteria floribunda agglutinin.

Table 2: PV neuron alterations in the hippocampus of stressed animals

Species	Age during manipulation	Age at measurement	Sex	Experimental paradigm	Brain Region	Method	Measure	Outcome	Reference
Mouse (C57/BL6)	Early postnatal	Early postnatal, juvenile, adolescent	♂	LB/LN P4-P11	Dentate Gyrus	IHC	PV cell density	Increased at P21	[8] Bath et al. (2017)
Rat (Lister-hooded)	Adolescent	Adolescent	♂♀	CUS 3 days	Infrapyramidal Dentate Gyrus	IHC	PV cell density	increased in males	[20] Brydges et al. (2018)
Rat (Lister-hooded)	Adolescent	Adolescent	♂♀	CUS 3 days	Suprapyramidal Dentate Gyrus	IHC	PV cell density	no change	[20] Brydges et al. (2018)
Rat (Wistar)	Adult	Adult	♂	CMS 9 weeks	Dorsal Dentate Gyrus	IHC	PV cell density	decreased	[29] Csabai et al. (2017)
Rat (Wistar)	Adult	Adult	♂	CMS 9 weeks	Ventral Dentate Gyrus	IHC	Total PV cell number	no change	[31] Czeh et al. (2015)
Rat (Wistar)	Adult	Adult	♂	CMS 9 weeks	Dorsal Dentate Gyrus	IHC	Total PV cell number	no change	[31] Czeh et al. (2015)
PV-Cre Mouse	Adolescent-adult	Adult	not stated	SI 8 weeks; 16 days rest and behavioral tests	Ventral Dentate Gyrus	IHC	PV cell density	no change	[33] Deng et al. (2020)
Rat (Sprague-Dawley)	Early postnatal	Early postnatal	♂	Handling and MS: 15 or 180 mins/day from P2-P14	Dentate Gyrus	IHC	Total PV cell number	no change	[36] Dricks (2016)
Rat (Wistar)	Adult	Adult	♂	SI 3 weeks	Dentate Gyrus	IHC	Total PV cell number	decreased	[43] Filipovic et al. (2017)
Rat (Wistar)	Adult	Adult	♂	Acute (2h cold or RS) or chronic (21 days SI) stress, or chronic stress with acute stress at the end of isolation	Dentate Gyrus	IHC	PV-immunoreactive number	decreased by isolation and combined isolation + acute stressors	[42] Filipovic et al. (2013)

Rat (Sprague-Dawley)	Early postnatal	Adolescent	♂	MS: 3h/day from P2-P14, or early handling P2-P14 (moved to different cage 15min/day)	Dentate Gyrus: Molecular layer, Granule cell layer, and Polymorphic layer	IHC	PV cell density	decreased in MS vs no handling in molecular layer	[50] Giachino et al. (2007)
Mouse (C57/BL6)	Adolescent	Adult	♂	Maternal stress: GD9 poly I:C injection (mimics infection); offspring exposed to 10 days variable unpredictable stress from P30-P40	Ventral Dentate Gyrus	IHC	Total PV cell number	decreased by poly I:C and stress but not either alone	[53] Giovanoli et al. (2014)
Mouse (C57/BL6)	Adolescent	Adult	♂	Maternal stress: GD9 poly I:C injection (mimics infection); offspring exposed to 10 days variable unpredictable stress from P30-P40	Dorsal Dentate Gyrus	IHC	Total PV cell number	no change	[53] Giovanoli et al. (2014)
Rat (Wistar)	Juvenile-adult	Adult	♂	SI 8 weeks	Dentate Gyrus	IHC	PV cell density	no change	[60] Greene et al. (2001)
Rat (Sprague-Dawley)	Juvenile-adult	Adult	♀	SI 11 weeks	Dentate Gyrus	IHC	PV cell density	decreased	[64] Harte et al. (2007)
Rat (Sprague-Dawley)	Adolescent-adult	Adult	♂	RS 6h/day 3 weeks	Dentate Gyrus	IHC	PV cell density	decreased	[69] Hu et al. (2010)
Rat (Sprague-Dawley)	Adult	Adult	♂	Gulf war illness model: 4 weeks daily: 5 mins RS, pyridostigmine bromide 1.3mg/kg oral, DEET 200ul 40mg/kg dermal, and permethrin 200ul 0.13mg/kg dermal.	Dentate Gyrus	IHC	Total PV cell number	decreased	[107] Megahed et al. (2014)
Mouse (C57/BL6)	Early postnatal	Adult	♂	MSEW: MS 4h/day from P2-P5, then 8h/day from P6-P16. MS pups weaned at P17, controls at P21	Ventral Dentate Gyrus	IHC	PV cell density	decreased	[116] Murthy et al. (2019)
Rat (Wistar)	Adult	Adult	♂	CMS 8 weeks	Dentate Gyrus hilus	IHC	PV cell density	no change	[121] Nieto-Gonzalez et al. (2015)
Rat (Wistar)	Adult	Adult	♂	CMS 8 weeks	Dentate Gyrus granule cell layer	IHC	PV cell density	no change	[121] Nieto-Gonzalez

									et al. (2015)
Rat (Wistar)	Adult	Adult	♂	CMS 8 weeks	Dentate Gyrus	IHC	PV cell density	no change	[121] Nieto-Gonzalez et al. (2015)
Rat (Wistar)	Adult	Adult	♂	CUS 16 days or CMS 8 weeks	Dentate Gyrus	IHC	PV cell density; PV cell surface area; PV fluorescence intensity	no change	[122] Nowak et al. (2010)
Rat (Sprague-Dawley)	Early postnatal	Juvenile	♂♀	MS 4h/day 19 days	Dentate Gyrus	IHC	8-oxo-dG+ fraction of PV cells; PV+ cell 8-oxo-dG intensity; PV cell number; PV intensity	increased 8-oxo-dG+ fraction; increased PV+ 8-oxo-dG in females vs males and increased PV intensity in males vs females	[158] Soares et al. (2020)
GAD67(+/-GFP) (HET) mice	-	Juvenile	♂	Maternal RS: 45 mins 3x/day from E15 to E17.5; BrdU injection IP once at E12 or E15	Dentate Gyrus	IHC	PV+/GFP+ cell density	no change	[168] Uchida et al. (2014)
Mouse (C57/BL6)	Juvenile-adolescent	Adolescent	♂	SI 5 weeks	Dentate Gyrus	IHC and WFA stain	PV cell density; PNN+ fraction of PV cells; PV fluorescence intensity; PV soma area	decreased (all)	[169] Ueno et al. (2017)
Mouse (C57/BL6)	Adolescent-adult	Adult	♂	CSIS 7 weeks. After stress, mice housed individually for 1 year	Dentate Gyrus	IHC	PV cell density	decreased	[178] Wang et al. (2019)
Mouse (C57/BL6)	Early postnatal	Adult	♂	MSEW: MS 4h/day from P2-P5, then 8h/day from P6-P16. MS pups weaned at P17, controls at P21	Ventral Dentate Gyrus	IHC	c-Fos+ fraction of PV cells	no change	[116] Murthy et al. (2019)
Rat (Sprague-Dawley)	Juvenile-Adult	Adult	♂	Forced swim, 3 30-minute elevated platform sessions, 2 hours RS. 32 days rest followed by 4 days of odor exposure preceding 45s underwater restraint trauma. 4 weeks later, odor re-exposure then elevated plus maze before sacrifice	Dorsal Dentate Gyrus	IHC	PV+/c-Fos+ cell density	no change	[141] Regev-Tsur et al. (2020)
Rat (Sprague-Dawley)	Juvenile-Adult	Adult	♂	Forced swim, 3 30-minute elevated platform sessions, 2 hours RS. 32 days rest followed by 4 days of odor exposure preceding 45s underwater	Ventral Dentate Gyrus	IHC	PV+/c-Fos+ cell density	no change	[141] Regev-Tsur et al. (2020)

				restraint trauma. 4 weeks later, odor re-exposure then elevated plus maze before sacrifice					
Mouse (C57/BL6)	Early postnatal	Adult	♂	MSEW: MS 4h/day from P2-P5, then 8h/day from P6-P16. MS pups weaned at P17, controls at P21	Ventral Dentate Gyrus Granule Cell Layer	IHC	WFA intensity in PV cells	increased	[116] Murthy et al. (2019)
Mouse (C57/BL6)	Early postnatal	Adult	♂	MSEW: MS 4h/day from P2-P5, then 8h/day from P6-P16. MS pups weaned at P17, controls at P21	Ventral Dentate Gyrus	IHC and WFA stain	Otx2 intensity in PV+/PNN+ cells and in PV+/PNN- cells	increased in PV+/PNN+ cells	[116] Murthy et al. (2019)
Rat (Tryon Maze Dull)	Adult	Adult	♂	CSD 8 days	Hidden blade of the Dentate Gyrus granular layer	IHC	Relative Optical Density of PV stain	no change	[86] Krugers et al. (1996)
Rat (Tryon Maze Dull)	Adult	Adult	♂	CSD 8 days	Outer blade of the Dentate Gyrus granular layer	IHC	Relative Optical Density of PV stain	no change	[86] Krugers et al. (1996)
Rat (Sprague-Dawley)	Adolescent	Adolescent	♀	RS 4h	Hilus subgranular zone	IHC; EM	mu-opioid receptor number in PV-labeled cell dendrites	decreased	[111] Milner et al. (2013)
Rat (Sprague-Dawley)	Adolescent	Adolescent	♀	RS 4h	Hilus subgranular zone	IHC; EM	mu-opioid receptor density in PV-labeled cell dendrite cytoplasm and plasma membrane	decreased in cytoplasm	[111] Milner et al. (2013)
Rat (Sprague-Dawley)	Adolescent	Adolescent	♀ (proestrus and estrus)	RS 4h	Hilus	IHC; EM	mu-opioid receptor density in PV-labeled cell small dendrite cytoplasm and plasma membrane	increased in proestrus plasma membrane; decreased in proestrus and estrus cytoplasm	[111] Milner et al. (2013)
Rat (Sprague-Dawley)	Adolescent	Adolescent	♂	RS 4h	Hilus	IHC; EM	mu-opioid receptor number in PV-labeled cell dendrites	no change	[111] Milner et al. (2013)
Rat (Sprague-Dawley)	Adolescent	Adolescent	♂♀	RS 4h/day for 10 days	Hilus	IHC	PV cell density	decreased in males	[111] Milner et al. (2013)
Rat (Sprague-Dawley)	Adolescent	Adolescent	♀ (estrus)	RS 4h/day for 10 days	Hilus	IHC	PV cell total dendrite area	decreased	[111] Milner et al. (2013)

Rat (Sprague-Dawley)	Adolescent	Adolescent	♀ (estrus)	RS 4h/day for 10 days	Hilus	IHC; EM	mu-opioid receptor density in PV-labeled cell dendrites	increased	[111] Milner et al. (2013)
Rat (Sprague-Dawley)	Adolescent	Adolescent	♂♀ (estrus)	RS 4h/day for 10 days	Hilus	IHC; EM	mu-opioid receptor density in PV-labeled cell dendrite cytoplasm	increased in females	[111] Milner et al. (2013)
Mouse (C57/BL6)	Adolescent	Adolescent	♂	RS 6h/day 3 weeks	CA1	IHC	Total PV cell number; PV cellular intensity	no change	[27] Clarke et al. (2018)
Rat (Wistar)	Adult	Adult	♂	CMS 9 weeks	Dorsal CA1	IHC	PV cell density	decreased	[29] Csabai et al. (2017)
Rat (Wistar)	Adult	Adult	♂	CMS 9 weeks	Ventral CA1	IHC	Total PV cell number	decreased	[31] Czeh et al. (2015)
Rat (Wistar)	Adult	Adult	♂	CMS 9 weeks	Dorsal CA1	IHC	Total PV cell number	decreased	[31] Czeh et al. (2015)
PV-Cre Mouse	Adolescent-adult	Adult	not stated	SI 8 weeks; 16 days rest and behavioral tests	Ventral CA1	IHC	PV cell density	decreased	[33] Deng et al. (2020)
Rat (Sprague-Dawley)	Early postnatal	Early postnatal	♂	Handling and MS: 15 or 180 mins/day from P2-P14	CA1	IHC	Total PV cell number	no change	[36] Dricks (2016)
Rat (Wistar)	Adult	Adult	♂	SI 3 weeks	CA1	IHC	Total PV cell number	decreased	[43] Filipovic et al. (2017)
Rat (Wistar)	Adult	Adult	♂	Acute (2h cold or RS) or chronic (21 days SI) stress, or chronic stress with acute stress at the end of isolation	CA1	IHC	PV-immunoreactive number	decreased by isolation and combined isolation + acute stressors	[42] Filipovic et al. (2013)
Mouse (C57/BL6)	Adolescent	Adult	♂	Maternal stress: GD9 poly I:C injection (mimics infection); offspring exposed to 10 days variable unpredictable stress from P30-P40	Ventral CA1-3	IHC	Total PV cell number	no change	[53] Giovanoli et al. (2014)
Mouse (C57/BL6)	Adolescent	Adult	♂	Maternal stress: GD9 poly I:C injection (mimics infection); offspring exposed to 10 days	Dorsal CA1-3	IHC	Total PV cell number	no change	[53] Giovanoli et al. (2014)

				variable unpredictable stress from P30-P40					
Rat (Wistar)	Juvenile-adult	Adult	♂	SI 8 weeks	CA1	IHC	PV cell density	no change	[60] Greene et al. (2001)
Rat (Sprague-Dawley)	Juvenile-adult	Adult	♀	SI 11 weeks	CA1	IHC	PV cell density	no change	[64] Harte et al. (2007)
Rat (Sprague-Dawley)	Adolescent-adult	Adult	♂	RS 6h/day 3 weeks	CA1	IHC	PV cell density	decreased	[69] Hu et al. (2010)
Rat (Wistar)	Adult	Adult	♂	SDPS: 5 days defeat then SI until measurement	CA1	IHC	PV cell density 72 hours and 2, 4, and 8 weeks after last defeat	no change	[85] Koskinen et al. (2020)
Rat (Tryon Maze Dull)	Adult	Adult	♂	CSD 8 days	CA1 pyramidal cell layer	IHC	Relative Optical Density of PV stain	no change	[86] Krugers et al. (1996)
Rat (Sprague-Dawley)	Adult	Adult	♂	Gulf war illness model: 4 weeks daily: 5 mins RS, pyridostigmine bromide 1.3mg/kg oral, DEET 200ul 40mg/kg dermal, and permethrin 200ul 0.13mg/kg dermal.	CA1/3	IHC	Total PV cell number	no change	[107] Megahed et al. (2014)
C57/BL6 mice	Early postnatal	Adult	♂	MSEW: MS 4h/day from P2-P5, then 8h/day from P6-P16. MS pups weaned at P17, controls at P21	Ventral CA1	IHC	PV cell density	no change	[116] Murthy et al. (2019)
GAD67(+/-GFP) (HET) mice	-	Juvenile	♂	Maternal RS: 45 mins 3x/day from E15 to E17.5; BrdU injection IP once at E12 or E15	CA1	IHC	PV+/GFP+ cell density	decreased	[168] Uchida et al. (2014)
Mouse (C57/BL6)	Juvenile-adolescent	Adolescent	♂	SI 5 weeks	CA1	IHC and WFA stain	PV cell density; PNN+ fraction of PV cells; PV fluorescence intensity; PV soma area	decreased PNN+ fraction of PV cells and PV fluorescence	[169] Ueno et al. (2017)
Mouse (C57/BL6)	Adolescent-adult	Adult	♂	CSIS 7 weeks. After stress, mice housed individually for 1 year	CA1	IHC	PV cell density	decreased	[178] Wang et al. (2019)
Rat (Sprague-Dawley)	Early postnatal	Juvenile	♂♀	MS 4h/day 19 days	CA1	IHC	8-oxo-dG+ fraction of PV cells; PV+ cell 8-oxo-dG intensity; PV cell number; PV intensity	increased 8-oxo-dG+ fraction; increased PV+ 8-oxo-dG in females vs males and increased PV	[158] Soares et al. (2020)

								intensity in males vs females	
Rat (Wistar)	Adult	Adult	♂	SDPS: 5 days defeat then SI until measurement	CA1	IHC	PV+/CSPG+ cell density 72 hours and 2, 4, and 8 weeks after last defeat	decreased at 72 hours; increased at 8 weeks	[85] Koskinen et al. (2020)
C57/BL6 mice	Early postnatal	Adult	♂	MSEW: MS 4h/day from P2-P5, then 8h/day from P6-P16. MS pups weaned at P17, controls at P21	Ventral CA1	IHC and WFA stain	WFA intensity in PV cells	no change	[116] Murthy et al. (2019)
Rat (Wistar)	Adult	Adult	♂	CUS 16 days or CMS 8 weeks	CA1	IHC	PV cell density; PV cell surface area; PV fluorescence intensity	no change	[122] Nowak et al. (2010)
Rat (Wistar)	Adult	Adult	♂	SDPS: 5 days defeat then 3 months SI; controls pair housed for 3 months	Dorsal CA1	IHC	PV+ fraction of CSPG+ cells; CSPG intensity in PV cells	increased PV+ fraction	[143] Riga et al. (2017)
Rat (Wistar)	Adult	Adult	♂	SDPS: 5 days defeat then 3 months SI; controls pair housed for 3 months	CA1 stratum pyramidale	IHC	CSPG+ fraction of PV cells; PV intensity in CSPG+ cells	increased PV intensity	[143] Riga et al. (2017)
Rat (Wistar)	Adult	Adult	♂	SDPS: 5 days defeat then 3 months SI; controls pair housed for 3 months	CA1 stratum pyramidale	IHC	Fraction of high-PV expressing and intermediate-low-PV expressing PV+/CSPG+ and PV+/CSPG- cells	increased high-PV expressing and decreased intermediate-low-PV expressing PV+/CSPG+ cells	[143] Riga et al. (2017)
Rat (Sprague-Dawley)	Adolescent-adult	Adult	♂	RS 6h/day 3 weeks	CA1	Electrophysiology	sIPSC frequency and amplitude on pyramidal neurons	increased frequency	[69] Hu et al. (2010)
C57/BL6 mice	Early postnatal	Adult	♂	MSEW: MS 4h/day from P2-P5, then 8h/day from P6-P16. MS pups weaned at P17, controls at P21	Ventral CA1	IHC	c-Fos+ fraction of PV cells	no change	[116] Murthy et al. (2019)
Rat (Wistar)	Adult	Adult	♂	SDPS: 5 days defeat then 3 months SI; controls pair housed for 3 months	CA1 stratum pyramidale	Electrophysiology	sIPSC frequency and amplitude on pyramidal neurons	decreased frequency	[143] Riga et al. (2017)
Rat (Wistar)	Adult	Adult	♂	CMS 9 weeks	Dorsal CA2/3	IHC	PV cell density	decreased	[29] Csabai et al. (2017)
Rat (Wistar)	Adult	Adult	♂	CMS 9 weeks	Ventral CA2/3	IHC	Total PV cell number	no change	[31] Czeh et al. (2015)

Rat (Wistar)	Adult	Adult	♂	CMS 9 weeks	Dorsal CA2/3	IHC	Total PV cell number	decreased	[31] Czeh et al. (2015)
PV-Cre Mouse	Adolescent-adult	Adult	not stated	SI 8 weeks; 16 days rest and behavioral tests	Ventral CA2/3	IHC	PV cell density	decreased	[33] Deng et al. (2020)
Rat (Sprague-Dawley)	Early postnatal	Early postnatal	♂	Handling and MS: 15 or 180 mins/day from P2-P14	CA2/3	IHC	Total PV cell number	no change	[36] Dricks (2016)
Rat (Wistar)	Adult	Adult	♂	SI 3 weeks	CA2	IHC	Total PV cell number	decreased	[43] Filipovic et al. (2017)
Rat (Sprague-Dawley)	Juvenile-adult	Adult	♀	SI 11 weeks	CA2/3	IHC	PV cell density	decreased	[64] Harte et al. (2007)
Rat (Sprague-Dawley)	Adolescent-adult	Adult	♂	RS 6h/day 3 weeks	CA2/3	IHC	PV cell density	decreased	[69] Hu et al. (2010)
Mouse (C57/BL6)	Adolescent	Adolescent	♂	RS 6h/day 3 weeks	CA3	IHC	Total PV cell number; PV cellular intensity	increased PV cell number	[27] Clarke et al. (2018)
Rat (Wistar)	Adult	Adult	♂	SI 3 weeks	CA3	IHC	Total PV cell number	decreased	[43] Filipovic et al. (2017)
Rat (Wistar)	Adult	Adult	♂	Acute (2h cold or RS) or chronic (21 days SI) stress, or chronic stress with acute stress at the end of isolation	CA3	IHC	PV-immunoreactive number	decreased by isolation and combined isolation + acute stressors	[42] Filipovic et al. (2013)
Rat (Wistar)	Juvenile-adult	Adult	♂	SI 8 weeks	CA3	IHC	PV cell density	no change	[60] Greene et al. (2001)
Rat (Tryon Maze Dull)	Adult	Adult	♂	CSD 8 days	CA3 pyramidal cell layer	IHC	Relative Optical Density of PV stain	no change	[86] Krugers et al. (1996)
Mouse (C57/BL6)	Early postnatal	Adult	♂	MSEW: MS 4h/day from P2-P5, then 8h/day from P6-P16. MS pups weaned at P17, controls at P21	Ventral CA3	IHC	PV cell density	no change	[116] Murthy et al. (2019)
Rat (Wistar)	Adult	Adult	♂	CUS 16 days or CMS 8 weeks	CA3	IHC	PV cell density; PV cell surface area; PV fluorescence intensity	no change	[122] Nowak et al. (2010)

Rat (Sprague-Dawley)	Early postnatal	Juvenile	♂♀	MS 4h/day 19 days	CA3	IHC	8-oxo-dG+ fraction of PV cells; PV+ cell 8-oxo-dG intensity; PV cell number; PV intensity	increased PV+ 8-oxo-dG in females vs males and increased PV intensity in males vs females	[158] Soares et al. (2020)
GAD67(+/-GFP) (HET) mice	-	Juvenile	♂	Maternal RS: 45 mins 3x/day from E15 to E17.5; BrdU injection IP once at E12 or E15	CA3	IHC	PV+/-GFP+ cell density	no change	[168] Uchida et al. (2014)
Mouse (C57/BL6)	Juvenile-adolescent	Adolescent	♂	SI 5 weeks	CA3	IHC and WFA stain	PV cell density; PNN+ fraction of PV cells; PV fluorescence intensity; PV soma area	decreased PV fluorescence and PV soma area	[169] Ueno et al. (2017)
Mouse (C57/BL6)	Adolescent-adult	Adult	♂	CSIS 7 weeks. After stress, mice housed individually for 1 year	CA3	IHC	PV cell density	decreased	[178] Wang et al. (2019)
PV-Cre Mouse	Adolescent-adult	Adult	not stated	SI 8 weeks; 16 days rest and behavioral tests	Ventral Hippocampus	IHC	PV cell density	decreased	[33] Deng et al. (2020)
PV-Cre Mouse	Adolescent-adult	Adult	not stated	SI 8 weeks; 16 days rest and behavioral tests	Dorsal Hippocampus	IHC	PV cell density	no change	[33] Deng et al. (2020)
Rat (Sprague-Dawley)	Early postnatal	Early postnatal	♂	Handling and MS: 15 or 180 mins/day from P2-P14	Hippocampus	IHC	Total PV cell number	no change	[36] Dricks (2016)
Rat (Sprague-Dawley)	Adult	Adult	♂	Gulf war illness model: 4 weeks daily: 5 mins RS, pyridostigmine bromide 1.3mg/kg oral, DEET 200ul 40mg/kg dermal, and permethrin 200ul 0.13mg/kg dermal.	Hippocampus	IHC	Total PV cell number	decreased	[107] Megahed et al. (2014)
Rat (Sprague-Dawley)	Adult	Adult	♂	RS: 6h/day for 10 days	Hippocampus	IHC and WFA stain	Total PV cell number; total PNN+/-PV+ cell number	no change	[138] Pesarico et al. (2019)
Mouse (C57/BL6)	Juvenile; adult	Adolescent; adult	♂	CUS 7 days	Hippocampus	IHC and WFA stain	PV cell density; PNN+ fraction of PV cells; PV+ fraction of PNNs; PV fluorescence; PV soma area	no change	[170] Ueno et al. (2018)
Rat (Sprague-Dawley)	Adolescent	Adolescent	♂	Daily FS 10 days, RS 1h on days 1, 2, and 10	Ventral Hippocampus	IHC	Total PV cell number	decreased	[56] Gomes et al. (2019)

Rat (Sprague-Dawley)	Adult	Adult	♂	Daily FS 10 days, RS 1h on days 1, 2, and 10	Ventral Hippocampus	IHC	Total PV cell number	decreased	[56] Gomes et al. (2019)
Rat (Sprague-Dawley)	Adolescent	Adolescent; adult	♂	Daily FS 10 days, RS 1h on days 1, 2, and 10	Ventral Hippocampus	IHC and WFA stain	Total PV/PNN+ cell number	decreased in adolescents	[56] Gomes et al. (2019)
Rat (Wistar)	Adult	Adult	♂	SDPS: 5 days defeat then 3 months SI; controls pair housed for 3 months. ChABC or penicillinase bilateral injection to dorsal hippocampus >2 months after last CSD day	Dorsal Hippocampus	IHC	PV+/PNN+ cell density	increased by CSD in penicillinase- but not chABC-treated rats; decreased by chABC treatment compared to penicillinase in both stressed and unstressed rats	[143] Riga et al. (2017)
Mouse (CD1)	Early postnatal	Early postnatal, juvenile	♂♀	24h MS on P4 with no food or water	Dorsal Hippocampus	IHC	PV cell density	decreased in left but not right dorsal hippocampus at both P14 and P28	[77] Katahira et al. (2018)
Rat (Sprague-Dawley)	Early postnatal	Juvenile, adolescent	♂	MS 4h/day from P2-P20	Hippocampus	IHC; Western blot	PV cell density; PV protein content	no change	[19] Brenhouse and Andersen (2011)
Rat (Sprague-Dawley)	Early postnatal	Adolescent	♂♀	MS 3h/day 3 weeks	Hippocampus	IHC; Western blot	PV immunoreactivity; PV cluster number; PV protein expression	decreased immunoreactivity and cluster number	[79] Kim et al. (2020)
GAD67-GFP Mouse (CD1)	-	Juvenile, adult	♂	Maternal stress: beginning on GD12, mothers received restraint stress 45 mins 3x/d during daylight under bright lights. Litters weaned at P24	Hippocampus	IHC; qPCR	PV+ fraction of GAD67:GFP+ cells; PV:GAD1 mRNA ratio	decreased PV+ fraction at both ages, increased PV mRNA at P150	[99] Lussier and Stevens (2016)
Rat (Wistar)	Adult	Adult	♂	CMS 7 weeks	Ventral Hippocampus	qPCR; Western blot	PV mRNA expression; PV protein content	no change	[144] Rossetti et al. (2018)
Rat (Wistar)	Adult	Adult	♂	CMS 7 weeks	Dorsal Hippocampus	qPCR; Western blot	PV mRNA expression; PV protein content	decreased mRNA and protein	[144] Rossetti et al. (2018)
Mouse (C57/BL6)	Early postnatal	Early postnatal, juvenile, adolescent	♂	LB/LN P4-P11	Hippocampus	qPCR	PV mRNA expression	increased at P12 and P16	[8] Bath et al. (2017)

Rat (Sprague-Dawley)	Adolescent-adult	Adult	♂	CUS 36 days	Hippocampus	Western blot	PV protein content	no change	[6] Banasr et al. (2017)
Rat (Wistar)	Adult	Adult	♂	SDPS: 5 days defeat then 3 months SI; controls pair housed for 3 months. ChABC or penicillinase bilateral injection to dorsal hippocampus >2 months after last CSD day	Dorsal Hippocampus	Electrophysiology	sIPSC frequency on pyramidal neurons	decreased by SDPS in penicillinase-treated rats; increased by chABC compared to penicillinase in SDPS rats	[143] Riga et al. (2017)
GAD67(+/-GFP) (HET) mice	-	Juvenile	♂	Maternal RS: 45 mins 3x/day from E15 to E17.5; BrdU injection IP once at E12 or E15	Subiculum	IHC	PV+/GFP+ cell density	no change	[168] Uchida et al. (2014)
Rat (Sprague-Dawley)	Early postnatal	Adolescent	♂	MS: 3h/day from P2-P14, or early handling P2-P14 (moved to different cage 15min/day)	Ammon's Horn	IHC	PV cell density	no change	[50] Giachino et al. (2007)

Mouse and rat life stages were defined as follows: P0-19 (postnatal day 0-19, where day of birth is P0; juvenile: P20-30; adolescent: P31-60; and adult: P61+.

Abbreviations: BrdU: bromodeoxyuridine; chABC: chondroitinase ABC; CMS: chronic mild stress; CSD: chronic social defeat; CSIS: chronic social instability stress; CSPG: chondroitin sulfate proteoglycan; CUS: chronic unpredictable stress; EM: electron microscopy; FS: foot shock; GD#: gestational day, where day of fertilization is GD0; HET: heterozygous; IHC: immunohistochemistry; IP: intraperitoneal; LB/LN: limited bedding/limited nesting; MS: maternal separation; MSEW: maternal separation with early weaning; qPCR: quantitative polymerase chain reaction; RS: restraint stress; SDPS: social defeat-prolonged stress; SI: social isolation; WFA: Wisteria floribunda agglutinin.

Table 3: PV neuron alterations in other brain regions of stressed animals

Species	Age during manipulation	Age at measurement	Sex	Experimental paradigm	Brain Region	Method	Measure	Outcome	Reference
Mouse (C57/BL6)	Adolescent	Adolescent	♂	RS 6h/day 3 weeks	Basolateral Amygdala	IHC	Total PV cell number; PV cellular intensity	no change	[27] Clarke et al. (2008)
Rat (Sprague-Dawley)	Early postnatal	Adolescent	♂	MS 3h/day or early handling 15 mins/day from P2-P14	Basolateral Amygdala Basal Nucleus	IHC	PV cell density	no change	[50] Giachino et al. (2007)
Rat (Sprague-Dawley)	Early postnatal	Adolescent	♂	MS 3h/day or early handling 15 mins/day from P2-P14	Basolateral Amygdala Lateral Nucleus	IHC	PV cell density	increased by early handling and MS	[50] Giachino et al. (2007)
Mouse (C57/BL6)	Early postnatal	Early postnatal; juvenile; adolescent; adult	♂♀	LB/LN 7 days	Basolateral Amygdala	IHC	PV cell density	increased in juveniles	[101] Manzano Nieves et al. (2020)
Rat (Long-Evans)	Early postnatal	Early postnatal	♂♀	LB/LN P8-P12	Anterior/Mid Basolateral Amygdala	IHC	PV cell density; PV stain intensity	no change	[149] Santiago et al. (2018)
Rat (Long-Evans)	Early postnatal	Early postnatal	♂♀	LB/LN P8-P12	Posterior Basolateral Amygdala	IHC	PV cell density; PV stain intensity	no change	[149] Santiago et al. (2018)
Rat (Long-Evans)	Early postnatal	Juvenile	♂♀	LB/LN P8-P12	Anterior/Mid Basolateral Amygdala	IHC	PV cell density; PV stain intensity	no change	[149] Santiago et al. (2018)
Rat (Long-Evans)	Early postnatal	Juvenile	♂♀	LB/LN P8-P12	Posterior Basolateral Amygdala	IHC	PV cell density; PV stain intensity	no change	[149] Santiago et al. (2018)
Mouse (C57/BL6)	Adolescent-adult	Adult	♂	CSIS 7 weeks. After stress, mice housed individually for 1 year	Basolateral Amygdala	IHC	PV cell density	no change	[178] Wang et al. (2019)
Rat (Sprague-Dawley)	Early postnatal	Juvenile	♂♀	MS 4h/day 19 days	Basolateral Amygdala	IHC	8-oxo-dG+ fraction of PV cells; PV+ cell 8-oxo-dG intensity; PV cell number; PV intensity	increased PV intensity; 8-oxo-dG+ fraction increased in females vs males	[158] Soares et al. (2020)

Rat (Sprague-Dawley)	Adult	Adult	♂	RS: 6h/day for 10 days	Basolateral Amygdala	IHC and WFA stain	Total PV cell number; Total PV+/PNN+ cell number	increased PV cell number	[137] Pesarico et al. (2019)
Rat (Sprague-Dawley)	Early postnatal	Juvenile	♂♀	MS 4h/day from P2-P20	Basolateral Amygdala	IHC and WFA stain	PV+/PNN+ cell density; PV cell density; PV+ PNN intensity; PNN+ PV intensity; PV intensity	no change	[51] Gildawie et al. (2019)
Rat (Sprague-Dawley)	Early postnatal	Adolescent	♂♀	MS 4h/day from P2-P20	Basolateral Amygdala	IHC and WFA stain	PV+/PNN+ cell density; PV cell density; PV+ PNN intensity; PNN+ PV intensity; PV intensity	increased PV cell density in males	[51] Gildawie et al. (2019)
Rat (Sprague-Dawley)	Early postnatal	Adult	♂♀	MS 4h/day from P2-P20	Basolateral Amygdala	IHC and WFA stain	PV+/PNN+ cell density; PV cell density; PV+ PNN intensity; PNN+ PV intensity; PV intensity	no change	[51] Gildawie et al. (2019)
Rat (Sprague-Dawley)	Early postnatal	Juvenile	♂	LB/LN 9 days	Left and Right Basolateral Amygdala	IHC; WFA stain	PV cell density; PV+/PNN+ cell density; Fos+ proportion of PV cells; Fos+ proportion of PV+/PNN+ cells	increased PV+/PNN+ cell density in left and right BLA, increased Fos+ proportion of PV cells in right BLA only	[61] Guadagno et al. (2020)
Rat (Sprague-Dawley)	Early postnatal	Juvenile	♀	LB/LN 9 days	Left and Right Basolateral Amygdala	IHC; WFA stain	PV cell density; PV+/PNN+ cell density; Fos+ proportion of PV cells; Fos+ proportion of PV+/PNN+ cells	no change	[61] Guadagno et al. (2020)
Rat (Sprague-Dawley)	Early postnatal; juvenile	Juvenile	♂	LB/LN 9 days; fear conditioning P28-29	Left and Right Basolateral Amygdala	IHC; WFA stain	Fos+ proportion of PV cells; Fos+ proportion of PV+/PNN+ cells	decreased Fos+ proportion of PV cells in right BLA	[61] Guadagno et al. (2020)
Rat (Sprague-Dawley)	Early postnatal; juvenile	Juvenile	♀	LB/LN 9 days; fear conditioning P28-29	Left and Right Basolateral Amygdala	IHC; WFA stain	Fos+ proportion of PV cells; Fos+ proportion of PV+/PNN+ cells	no change	[61] Guadagno et al. (2020)
Rat (Sprague-Dawley)	Adolescent	Adult	♀	SI from P21-P42, then 20 days of group housing (isolates together, non-isolates together). On P62, anxiogen FG-7142 injection 2 hours before sacrifice to provoke c-Fos expression in the amygdala	Anterior Basolateral Amygdala	IHC	Total PV cell number; total PV+/c-Fos+ cell number	decreased PV+/c-Fos+ cell number	[96] Lukkes et al. (2012)
Rat (Sprague-Dawley)	Adolescent	Adult	♀	SI from P21-P42, then 20 days of group housing	Posterior Basolateral Amygdala	IHC	Total PV cell number; total PV+/c-Fos+ cell number	no change	[96] Lukkes et al. (2012)

				(isolates together, non-isolates together). On P62, anxiogen FG-7142 injection 2 hours before sacrifice to provoke c-Fos expression in the amygdala					
Rat (Sprague-Dawley)	Adult	Adult	♂	RS: 6h/day for 10 days. Acute RS 2h on day 11 then sacrifice	Basolateral Amygdala	IHC	PV cell density; c-Fos+ fraction of PV cells	c-Fos+ fraction of PV cells increased by acute stress and chronic + acute stress, decreased by chronic restraint alone	[142] Reznikov et al. (2008)
Rat (Sprague-Dawley)	Juvenile	Adolescent	♀	1 week SI	Basolateral Amygdala	IHC; WFA stain	c-Fos+ proportion of PV cells; WFA+ proportion of PV cells; c-Fos+ proportion of WFA+ PV cells	decreased WFA+ proportion; increased c-Fos+ proportion of WFA+ PV cells	[173] Vazquez-Sanroman et al. (2020)
Erbin KO Mouse (C57/BL6)	Adult	Adult	♂	RS 2h/day for 3 days	Basolateral Amygdala	Electrophysiology	ratio of AMPA:NMDA currents in PV cells; eIPSC amplitude in PV neurons; mEPSC amplitude in PV neurons; mEPSC frequency in PV neurons	decreased AMPA:NMDA ratio and mEPSC amplitude	[98] Luo et al. (2019)
Rat (Wistar)	Early postnatal; adult	Adult	♂	Open field stress under bright light 15 mins/day from P0-P20, then on P90	Basolateral Amygdala	IHC	PV+/c-Fos+ cell density	no change	[38] Ebertowska et al. (2020)
Rat (Sprague-Dawley)	Juvenile-Adult	Adult	♂	Forced swim, 3 30-minute elevated platform sessions, 2 hours RS. 32 days rest followed by 4 days of odor exposure preceding 45s underwater restraint trauma. 4 weeks later, odor re-exposure then elevated plus maze before sacrifice	Basolateral Amygdala	IHC	PV+/c-Fos+ cell density	increased in affected vs unaffected rats and control	[141] Regev-Tsur et al. (2020)
Rat (Sprague-Dawley)	Juvenile	Juvenile	♂	RS and LH 2h/day P22-24	Basolateral Amygdala	Electrophysiological recordings from pyramidal neurons	Frequency, amplitude, rise time, and decay time of sIPSCs	no change	[74] Jiang et al. (2009)
Rat (Sprague-Dawley)	Juvenile	Juvenile	♂	RS and LH 2h/day P22-24	Basolateral Amygdala	alpha-methyl-5-HT application; electrophysiological	sIPSC frequency	decreased	[74] Jiang et al. (2009)

						recording from pyramidal neurons			
Rat (Sprague-Dawley)	Early postnatal; adolescent	Adolescent	♀	MS 4h/day from P2-P20; LH task P41	Basolateral Amygdala	Western blot	PV protein content	no change	[96] Lukkes et al. (2017)
Rat (Sprague-Dawley)	Early postnatal; adolescent	Adolescent	♀	MS 4h/day from P2-P20; LH task P41; allowed to witness another rat in task 1d before they did it.	Basolateral Amygdala	Western blot	PV protein content	decreased	[96] Lukkes et al. (2017)
PV-Cre Mouse (C57/BL6)	Adult	Adult	♂	RS 2h/day for 3 days	Basolateral Amygdala	FACS-qPCR	PV cell mRNA expression of fgfr2, fgf13, Nrg1, Narp, PSD95, Erbin, ErbB2, ErbB4, GluA1, GluA2	decreased Erbin expression	[98] Luo et al. (2019)
Rat (Long-Evans)	Early postnatal	Juvenile	♂♀	LB/LN P8-P12	Basolateral Amygdala	EM stains for PV and excitatory synapse terminals	Percentage of pyramidal neuron membrane receiving contact from PV terminals; PV terminal number per um of pyramidal cell membrane; average length of PV terminal contacts onto pyramidal cells	decreased (all 3)	[149] Santiago et al. (2018)
Rat (Long-Evans)	Early postnatal	Juvenile	♂♀	LB/LN P8-P12	Basolateral Amygdala	EM stains for PV and excitatory synapse terminals	Percentage of PV cell membrane contacted by PV and excitatory terminals; PV and excitatory terminal number/um of PV cell membrane; excitatory terminal length onto PV cells	decreased percentage of membrane contact by PV cells; decreased PV terminal number per um of membrane	[149] Santiago et al. (2018)
Rat (Wistar)	Early postnatal; adult	Adult	♂	Open field stress under bright light 15 mins/day from P0-P20, then on P90	Lateral Amygdala	IHC	c-Fos+/PV+ cell density	decreased	[38] Ebertowska et al. (2020)
Rat (Sprague-Dawley)	Adolescent	Adult	♀	SI from P21-P42, then 20 days of group housing (isolates together, non-isolates together). On P62, anxiogen FG-7142 injection 2 hours before sacrifice to provoke c-Fos expression in the amygdala	Ventrolateral Lateral Amygdala	IHC	Total PV cell number; total PV+/c-Fos+ cell number	no change	[96] Lukkes et al. (2012)

Rat (Sprague-Dawley)	Adolescent	Adult	♀	SI from P21-P42, then 20 days of group housing (isolates together, non-isolates together). On P62, anxiogen FG-7142 injection 2 hours before sacrifice to provoke c-Fos expression in the amygdala	Ventromedial Lateral Amygdala	IHC	Total PV cell number; total PV+/c-Fos+ cell number	no change	[96] Lukkes et al. (2012)
Rat (Sprague-Dawley)	Adolescent	Adult	♀	SI from P21-P42, then 20 days of group housing (isolates together, non-isolates together). On P62, anxiogen FG-7142 injection 2 hours before sacrifice to provoke c-Fos expression in the amygdala	Dorsolateral Lateral Amygdala	IHC	Total PV cell number; total PV+/c-Fos+ cell number	decreased PV+/c-Fos+ cell number	[96] Lukkes et al. (2012)
Rat (Sprague-Dawley)	Juvenile-Adult	Adult	♂	Forced swim, 3 30-minute elevated platform sessions, 2 hours RS. 32 days rest followed by 4 days of odor exposure preceding 45s underwater restraint trauma. 4 weeks later, odor re-exposure then elevated plus maze before sacrifice	Central Amygdala	IHC	PV+/c-Fos+ cell density	no change	[141] Regev-Tsur et al. (2020)
Mouse (C57/BL6)	Adolescent-adult	Adult	♂	CSIS 7 weeks. After stress, mice housed individually for 1 year	Central Amygdala	IHC	PV cell density	no change	[178] Wang et al. (2019)
Rat (Wistar)	Early postnatal; adult	Adult	♂	Open field stress under bright light 15 mins/day from P0-P20, then on P90	Posterolateral Cortical Amygdala	IHC	c-Fos+/PV+ cell density	no change	[38] Ebertowska et al. (2020)
Rat (Sprague-Dawley)	Early postnatal; adolescent	Adolescent	♀	MS 4h/day from P2-P20; LH tests P40-41	Amygdala	Western blot	PV protein content	decreased in anhedonic vs non-anhedonic	[97] Lukkes et al. (2018)
Rat (Sprague-Dawley)	Juvenile-adolescent	Adolescent	♀	SI 3 weeks	Amygdala	Western blot	PV protein content	decreased in anhedonic vs non-anhedonic	[97] Lukkes et al. (2018)
Mouse (C57/BL6)	Early postnatal	Adult	♂♀	LB/LN	Orbitofrontal cortex	qPCR	PV mRNA expression	decreased	[58] Goodwill et al. (2018)

Mouse (C57/BL6)	Early postnatal	Adult	♂♀	LB/LN	Ventral Orbitofrontal cortex	IHC	PV cell density	decreased in females	[58] Goodwill et al. (2018)
Mouse (C57/BL6)	Early postnatal	Adult	♂♀	LB/LN	Lateral Orbitofrontal cortex	IHC	PV cell density	decreased in females	[58] Goodwill et al. (2018)
Rat (Wistar)	Adolescent	Adolescent	♂	CMS 4 days	Dorsolateral Orbitofrontal cortex	IHC	PV cell density	no change	[173] Varga et al. (2016)
Rat (Wistar)	Adolescent	Adolescent	♂	CMS 4 days	Lateral Orbitofrontal cortex	IHC	PV cell density	no change	[173] Varga et al. (2016)
Rat (Wistar)	Adolescent	Adolescent	♂	CMS 4 days	Medial Orbitofrontal cortex	IHC	PV cell density	no change	[173] Varga et al. (2016)
Rat (Wistar)	Adolescent	Adolescent	♂	CMS 4 days	Ventral Orbitofrontal cortex	IHC	PV cell density	no change	[173] Varga et al. (2016)
Mouse (C57/BL6)	Adolescent	Adolescent	♂♀	RS 2h/day for 7 days	Barrel cortex	IHC	PV cell density; c-Fos+ fraction of PV cells	decreased c-Fos+ fraction of PV cells	[23] Chen et al. (2018)
PV-Cre Mouse (C57/BL6)	Adolescent	Adolescent	♂♀	RS 2h/day for 7 days	Barrel cortex	Optogenetic stimulation of PV cells; slice electrophysiology recording from pyramidal neurons	oIPSC amplitude	no change	[23] Chen et al. (2018)
PV-Cre Mouse (C57/BL6)	Adolescent	Adolescent	♂♀	RS 2h/day for 7 days	Barrel cortex	Current injection to and electrophysiological recording from PV cells	Firing frequency	decreased at high (≥ 300 pA) but not low current injection	[23] Chen et al. (2018)
PV-Cre Mouse (C57/BL6)	Adolescent	Adolescent	♂♀	Cre-dependent DREADD injection to bilateral barrel cortex; 7 days of CNO injection then RS 2h/day	Barrel cortex	DREADD activation of PV cells; IHC	Dendritic spine formation and elimination	decreased elimination	[23] Chen et al. (2018)
Mouse (C57/BL6)	Early postnatal	Adult	♂♀	LB/LN from P4-P11	Primary Somatosensory cortex	qPCR	PV mRNA expression	no change	[58] Goodwill et al. (2018)
GAD67(+/-GFP) (HET) mouse	-	Juvenile	♂	Maternal RS: 45 mins 3x/day from E15 to E17.5; BrdU injection IP once at E12 or E15	Primary Somatosensory cortex - 10 sagittal sections	IHC	PV+/GFP+ cell density	decreased in section 4	[168] Uchida et al. (2014)
Rat (Sprague-Dawley)	Adult	Adult	♂	RS 2h/day for 3 weeks	Somatosensory cortex	IHC	PV cell density	decreased	[89] Lee et al. (2015)

Mouse (C57/BL6)	Juvenile-adolescent	Adolescent	♂	SI 5 weeks	Somatosensory cortex layers 2/3, 4, and 5/6	IHC and WFA stain	PV cell density; PNN+ fraction of PV cells; PV fluorescence intensity; PV soma area	no change	[169] Ueno et al. (2017)
Mouse (C57/BL6)	Juvenile-adolescent	Adolescent	♂	SI 5 weeks	Motor cortex layers 2/3 and 5/6	IHC and WFA stain	PV cell density; PNN+ fraction of PV cells; PV fluorescence intensity; PV soma area	no change	[169] Ueno et al. (2017)
Mouse (C57/BL6)	Juvenile; adult	Adolescent; adult	♂	CUS 7 days	Primary Motor cortex	IHC and WFA stain	PV cell density; PNN+ fraction of PV cells; PV+ fraction of PNNs; PV fluorescence; PV soma area	no change	[170] Ueno et al. (2018)
Rat (Wistar)	Adolescent	Adolescent	♂	CMS 4 days	Primary Motor cortex	IHC	PV cell density	no change	[173] Varga et al. (2016)
Mouse (C57/BL6)	Adult	Adult	♂♀	3 weeks UCMS	Nucleus Accumbens Shell	Patch clamp	100pA current injection-induced PV cell firing frequency; resting PV cell membrane potential; PV cell action potential threshold	increased firing frequency	[183] Xiao et al. (2020)
Rat (Sprague-Dawley)	Adult	Adult	♂	RS: 6h/day for 10 days	Thalamic Reticular Nucleus	IHC	PV stain intensity	increased	[138] Pesarico et al. (2019)
Rat (Sprague-Dawley)	Adult	Adult	♂	RS 6h/day for 10 days	Habenula	IHC	PV stain intensity	increased	[138] Pesarico et al. (2019)
Rat (Sprague-Dawley)	Early postnatal; adolescent	Adolescent	♀	MS 4h/day from P2-P20; LH task P41	Dorsal Raphe Nucleus	Western blot	PV protein content	decreased	[96] Lukkes et al. (2017)
Rat (Sprague-Dawley)	Early postnatal; adolescent	Adolescent	♀	MS 4h/day from P2-P20; LH task P41; allowed to witness another rat in task 1 day before they did it.	Dorsal Raphe Nucleus	Western blot	PV protein content	no change	[96] Lukkes et al. (2017)
Mouse (C57/BL6)	Juvenile-adult	Adolescent	♂	SI 5 weeks	Visual cortex layers 2/3, 4 and 5/6	IHC and WFA stain	PV cell density; PNN+ fraction of PV cells; PV fluorescence intensity; PV soma area	decreased PNN+ fraction of PV cells in layer 2/3	[169] Ueno et al. (2017)
Mouse (C57/BL6)	Juvenile-adult	Adolescent	♂	SI 5 weeks	Perirhinal cortex	IHC and WFA stain	PV cell density; PNN+ fraction of PV cells; PV fluorescence intensity; PV soma area	decreased PV fluorescence intensity	[169] Ueno et al. (2017)

Mouse (C57/BL6)	Juvenile-adult	Adolescent	♂	SI 5 weeks	Dorsintermed Entorhinal cortex	IHC and WFA stain	PV cell density; PNN+ fraction of PV cells; PV fluorescence intensity; PV soma area	no change	[169] Ueno et al. (2017)
Mouse (C57/BL6)	Juvenile-adult	Adolescent	♂	SI 5 weeks	Dorsolateral Entorhinal cortex	IHC and WFA stain	PV cell density; PNN+ fraction of PV cells; PV fluorescence intensity; PV soma area	decreased PV fluorescence intensity	[169] Ueno et al. (2017)

Mouse and rat life stages were defined as the following: early postnatal: P0-19 (postnatal day 0-19, where day of birth is P0; juvenile: P20-30; adolescent: P31-60; and adult: P61+. Abbreviations: CMS: chronic mild stress; CNO: clozapine N-oxide; CSD: chronic social defeat; CSIS: chronic social instability stress; CUS: chronic unpredictable stress; EM: electron microscopy; FACS: flow-associated cell sorting; HET: heterozygous; IHC: immunohistochemistry; IP: intraperitoneal; KO: knockout; LB/LN: limited bedding/limited nesting; LH: learned helplessness; LHb: lateral habenula; MS: maternal separation; qPCR: quantitative polymerase chain reaction; RS: restraint stress; SI: social isolation; VTA: ventral tegmental area; WFA: Wisteria floribunda agglutinin.

Table 4: Animal PV neuron alterations under enrichment paradigms

Species	Age during manipulation	Age at measurement	Sex	Experimental paradigm	Brain region	Method	Measure	Outcome	Reference
Rat (Sprague-Dawley)	Early postnatal; adolescent	Adolescent	♂	MS 4h/day; 500uM TAT2A microinjection into PFC every other day from P31-P39	Prelimbic cortex	IHC	PV cell density	rescued MS-induced decrease	[48] Ganguly et al. (2015)
Rat (Sprague-Dawley)	Early postnatal	Juvenile; adult	♂	Oral FLX 10mg/kg/d from P2-P21	Prelimbic cortex	IHC; WFA stain	PV cell density	no change	[113] Mukhopadhyay et al. (2020)
Rat (Wistar)	Adult	Adult	♂	EE 2 months	Prelimbic cortex	IHC	Total PV cell number	increased	[148] Sampedro-Piquero et al. (2016)
Rat (Sprague-Dawley)	Adult	Adult	♂	FLX 10mg/kg twice daily IP for 15 days, then brains collected on day 35	Prelimbic cortex	IHC	PV cell density	decreased	[159] Song et al. (2019)
Rat (Wistar)	Adult	Adult	♂	SI 21 days; FLX 15mg/kg/day, CLZ 20mg/kg/day, or vehicle IP during stress.	Prelimbic cortex	IHC	Total PV cell number	decreased by SI in vehicle but not CLZ or FLX treatment	[166] Todorovic et al. (2018)
Rat (Sprague-Dawley)	Adolescent	Adolescent	♂	R- or S-ketamine 10mg/kg IP; sacrifice 30 mins later	Prelimbic cortex	IHC	PV cell density	Decreased by S-ketamine	[185] Yang et al. (2015)
Rat (Sprague-Dawley)	Early postnatal; adolescent	Adolescent	♂	MS 4h/day P2-P20; IL-10 intraventricular infusion from P30-P38. Sacrifice on P40	Prelimbic cortex	IHC	PV cell density; fraction of PV cells co-expressing NR2A	density decreased by MS, rescued by IL-10; fraction increased by MS, rescued by IL-10	[181] Wieck et al. (2013)
Rat (Sprague-Dawley)	Juvenile-adolescent	Adolescent	♂♀	EE P21-P36	Prelimbic cortex	Western blot	PV protein content	no change	[34] do Prado et al. (2015)
Rat (Sprague-Dawley)	Early postnatal-adolescent	Adolescent	♂♀	MS 4h/day from P2-P20; EE P21-P36	Prelimbic cortex	Western blot	PV protein content	decreased in males	[34] do Prado et al. (2015)
Rat (Sprague-Dawley)	Early postnatal; adolescent	Adolescent	♂	MS 4h/day; 500uM TAT2A microinjection into PFC every other day from P31-P39	Infralimbic cortex	IHC	PV cell density	rescued MS-induced decrease	[48] Ganguly et al. (2015)

Rat (Sprague-Dawley)	Early postnatal	Juvenile; adult	♂	Oral FLX 10mg/kg/d from P2-P21	Infralimbic cortex	IHC; WFA stain	PV cell density	no change	[113] Mukhopadhyay et al. (2020)
Rat (Wistar)	Adult	Adult	♂	EE 2 months	Infralimbic cortex	IHC	Total PV cell number	no change	[148] Sampedro-Piquero et al. (2016)
Rat (Sprague-Dawley)	Adult	Adult	♂	FLX 10mg/kg twice daily IP for 15 days, then brains collected on day 35	Infralimbic cortex	IHC	PV cell density	decreased	[159] Song et al. (2019)
Rat (Wistar)	Adult	Adult	♂	SI 21 days; FLX 15mg/kg/day, CLZ 20mg/kg/day, or vehicle IP during stress.	Infralimbic cortex	IHC	Total PV cell number	decreased by SI in vehicle but not CLZ or FLX treatment	[166] Todorovic et al. (2018)
Rat (Sprague-Dawley)	Adolescent	Adolescent	♂	R- or S-ketamine 10mg/kg IP; sacrifice 30 mins later	Infralimbic cortex	IHC	PV cell density	no change	[185] Yang et al. (2015)
Mouse (C57/BL6)	Adult	Adult	♂	10mg/kg/d oral FLX 30 days	Infralimbic cortex	IHC; WFA stain	PV+ fraction of PNN+ cells	no change	[76] Karpova et al. (2014)
Rat (Sprague-Dawley)	Juvenile-adolescent	Adolescent	♂♀	EE P21-P36	Infralimbic cortex	Western blot	PV protein content	no change	[34] do Prado et al. (2015)
Rat (Sprague-Dawley)	Early postnatal-adolescent	Adolescent	♂♀	MS 4h/day from P2-P20; EE P21-P36	Infralimbic cortex	Western blot	PV protein content	decreased in males	[34] do Prado et al. (2015)
Rat (Sprague-Dawley)	Early postnatal	Juvenile; adult	♂	Oral FLX 10mg/kg/d from P2-P21	Cingulate cortex	IHC; WFA stain	PV cell density	no change	[113] Mukhopadhyay et al. (2020)
Mouse (C57/BL6)	Adolescent-adult	Adult	♂	Dried bonito broth (10%) intake 53 days	Medial Prefrontal cortex	IHC	PV cell density	increased	[73] Jargalsaikhan et al. (2016)
Rat (Wistar)	Adult	Adult	♂	SI 21 days; FLX 15mg/kg/day, CLZ 20mg/kg/day, or vehicle IP during stress.	Medial Prefrontal cortex	IHC	Total PV cell number	decreased by SI in vehicle but not CLZ or FLX treatment	[165] Todorovic et al. (2018)
Mouse (C57/BL6)	Adult	Adult	♂	FLX 15mg/kg/day IP for 3 weeks	Medial Frontal cortex	IHC and WFA stain	PV cell density; PV+/PNN+ cell density; PNN+ fraction of PV cells	decreased (all)	[124] Ohira et al. (2013)
Mouse (GAD-GFP)	Adult	Adult	♂	IP injection of 20mg/kg FLX daily for 2 weeks	Medial Prefrontal cortex	IHC; WFA stain	Total PV cell number; total PV+/PNN+ cell number; PV+ fraction of PNN+ cells;	decreased PV+/PNN+ cell number; decreased	[62] Guirado et al. (2014)

							perisomatic PV, synaptophysin, and PV+/synaptophysin+ puncta densities on pyramidal cells	perisomatic PV+/synaptophysin+ puncta	
Rat (Wistar)	Juvenile-adult	Adult	♂♀	SI 7 weeks with 5mg/kg/day oral apocynin	Prefrontal cortex	IHC	PV immunoreactivity	decreased by SI alone, no change in apocynin alone or SI + apocynin	[150] Schiavone et al. (2009)
Rat (Wistar)	Adult	Adult	♂	Ketamine 10mg/kg IP; brains harvested 0.5 and 2h after	Prefrontal cortex	IHC	PV fluorescence intensity	decreased 0.5h but not 2h after ketamine treatment	[189] Zhou et al. (2014)
Rat (Wistar)	Adult	Adult	♂	Apocynin 5mg/kg/day oral for 7 days; ketamine 10mg/kg IP on day 8; brains harvested 0.5 and 2h after ketamine	Prefrontal cortex	IHC	PV fluorescence intensity	decreased by ketamine alone but not apocynin + ketamine	[189] Zhou et al. (2014)
Rat (Sprague-Dawley)	Early postnatal; adolescent	Adolescent	♀	MS 4h/day; treatment with COX-2 inhibitor NS-398 (8mg/kg) every other day IP from P30-P38; LH task P41	Prefrontal cortex	Western blot	PV protein content	increased	[96] Lukkes et al. (2017)
Rat (Sprague-Dawley)	Early postnatal; adolescent	Adolescent	♀	MS 4h/day; treatment with COX-2 inhibitor NS-398 (8mg/kg) every other day IP from P30-P38; LH P41; allowed to witness another rat in task 1 day before they did it.	Prefrontal cortex	Western blot	PV protein content	no change	[96] Lukkes et al. (2017)
Rat (Wistar)	Juvenile-adult	Adult	♂♀	SI 7 weeks with 5mg/kg/day oral apocynin	Prefrontal cortex	Western blot	PV protein content	decreased by SI alone, no change in apocynin alone or SI + apocynin	[150] Schiavone et al. (2009)
Rat (Sprague-Dawley)	Adult	Adult	♂	IFS 15 mins on day 0, then EE 2h/day for 30 days. Brains collected on day 46	Prefrontal cortex	Western blot	PV protein content	IFS reduced PV protein, EE + IFS rescued normal amount. No change for EE alone	[163] Sun et al. (2016)
Rat (Wistar)	Adult	Adult	♂	Neuregulin-1 infusion to lateral ventricles same time as ketamine 10mg/kg IP	Prefrontal cortex	Western blot	PV protein content	decreased by ketamine but not ketamine + neuregulin-1	[178] Wang et al. (2014)
Rat (Wistar)	Adult	Adult	♂	Ketamine 10mg/kg IP; brains harvested 0.5 and 2h after	Prefrontal cortex	Western blot	PV protein content	decreased 0.5h but not 2h after ketamine treatment	[189] Zhou et al. (2014)
Mouse (C57/BL6)	Adult	Adult	♂♀	10mg/kg ketamine IP; 1 week rest	Prefrontal Cortex	qPCR	PV mRNA expression	decreased in males	[126] Okine et al. (2020)
Mouse (C57/BL6)	Adult	Adult	♂♀	10mg/kg ketamine IP; 1 week rest; 4 weeks UCMS	Prefrontal Cortex	qPCR	PV mRNA expression	decreased in males	[126] Okine et al. (2020)

Rat (Wistar)	Adult	Adult	♂	Lurasidone 3mg/kg/day oral for 5 weeks	Prefrontal cortex	qPCR	PV mRNA expression	no change	[144] Rossetti et al. (2018)
Rat (Wistar)	Adult	Adult	♂	CMS 7 weeks + lurasidone 3mg/kg/day oral during last 5 weeks of CMS	Prefrontal cortex	qPCR	PV mRNA expression	no change	[144] Rossetti et al. (2018)
Mouse (C57/BL6)	Adolescent	Adolescent	♂♀	10uM ketamine bath application	Frontal Association cortex	Electrophysiology	PV cell firing frequency 10, 30, and 50 mins after ketamine infusion	increased after ketamine at injected currents of 50, 100, 150, 200, and 250 pA	[119] Ng et al. (2018)
PV-Cre;Ai9-tdTomato Mice (C57/BL6); AAV injection of Cre-GCaMP6f	Adolescent	Adolescent	♂♀	8 hours RS; 10mg/kg IP ketamine at 4 and 8 hour marks	Frontal Association cortex layers 2/3	GCaMP6f signal recording	PV cell intracellular calcium (average $\Delta F/F_0$)	increased by RS + ketamine vs RS + saline	[119] Ng et al. (2018)
Mouse (C57/BL6)	Adolescent	Adolescent	♂♀	10mg/kg IP ketamine or saline, followed by 6h RS for 1, 2, 5, or 7 days	Frontal Association cortex layers 2/3	In vivo PV axonal bouton imaging	PV bouton elimination, formation, and net change in PV bouton number	increased elimination at day 7 RS vs no RS; decreased formation at day 5 and day 7 RS vs RS + ketamine; decreased net change in PV bouton number at day 5 and 7 RS compared to no RS group.	[119] Ng et al. (2018)
PV-Cre;Ai9-tdTomato Mice (C57/BL6)	Adolescent	Adolescent	♂♀	CNO and ketamine 10mg/kg injection into PV-hM3D or PV hM4D rats, followed by 6h RS, for 2 days	Frontal Association cortex layers 2/3	DREADD activation/inhibition of PV cells; Microscopy	PV cell dendritic spine elimination rate	increased by PV cell inhibition	[119] Ng et al. (2018)
PV-Cre;Ai9-tdTomato Mice (C57/BL6)	Adolescent	Adolescent	♂♀	CNO and ketamine 10mg/kg injection into PV-hM3D or PV hM4D rats, followed by 6h RS, for 2 days	Frontal Association cortex layers 2/3	DREADD activation/inhibition of PV cells; Microscopy	PV cell dendritic mushroom, stubby, and thin spine elimination rate	increased mushroom spine elimination in PV-inhibited mice	[119] Ng et al. (2018)
Rat (Wistar)	Adult	Adult	♂	EE 2 months	Cingulate cortex	IHC	Total PV cell number	increased	[148] Sampedro-Piquero et al. (2016)
Rat (Wistar)	Adult	Adult	♂	SI 21 days; FLX 15mg/kg/day, CLZ 20mg/kg/day, or vehicle IP during stress.	Cingulate cortex	IHC	Total PV cell number	decreased by SI, SI+FLX, and SI+CLZ	[166] Todorovic et al. (2018)

Rat (Wistar)	Adult	Adult	♂	SI 21 days; FLX 15mg/kg/day, CLZ 20mg/kg/day, or vehicle IP during stress.	Dorsal Peduncular cortex	IHC	Total PV cell number	decreased by SI in vehicle but not CLZ or FLX txt; increased by CLZ alone vs CLZ + SI	[166] Todorovic et al. (2018)
Wnt3a-Cre Mice (C57/BL6 * NZB)	Not stated	Adolescent	♂♀	EE: running wheel and Enviro-Dri bedding added (timeline not stated)	Dentate Gyrus	IHC	PV cell density	no change	[4] Anstotz et al. (2018)
Tree Shrew (Tupaia Belangeri)	Adult	Adult	♂	5 weeks' daily psychosocial conflict; FLX (15mg/kg/day) or SLV-323 (20mg/kg/day) oral treatment daily for latter 4 weeks	Dentate Gyrus	IHC	Total PV cell number	Decreased by stress; rescued by FLX and by SLV-323	[30] Czeh et al. (2005)
Rat (Wistar)	Adolescent-adult	Adult	♂	FLX 15mg/kg/day or CLZ 20mg/kg/day with SI for 3 weeks	Dentate Gyrus	IHC	Total PV cell number	decreased by FLX + SI compared to SI	[43] Filipovic et al. (2017)
Rat (Wistar)	Juvenile-adolescent	Adult	♂	Physical exercise 40 days	Dentate Gyrus	IHC	Total PV cell number	no change	[57] Gomes da Silva et al. (2010)
Rat (Wistar)	Adolescent-adult	Adult	♂	CUS 3 weeks. Anhedonic subgroup given escitalopram (5mg/kg/day) or vehicle IP for 5 weeks	Dentate gyrus hilus and granule cell layer	IHC	PV cell density	no change	[68] Holm et al. (2011)
Rat (Long-Evans)	Adult	Adult	♂	Physical exercise 30 min/day for 5 weeks	Dentate Gyrus	IHC	Total PV cell number	no change	[120] Nguyen et al. (2013)
Rat (Wistar)	Adult	Adult	♂	SI 6 weeks with anhedonic rats given tianeptine 10mg/kg/day IP for last 3 weeks	Dentate Gyrus	IHC	Total PV cell number	increased by tianeptine + SI vs SI alone	[135] Peric et al. (2018)
Rat (Wistar)	Adult	Adult	♂	EE 2 months	Dentate Gyrus	IHC	Total PV cell number	no change	[148] Sampedro-Piquero et al. (2016)
Rat (Wistar)	Juvenile	Adult	♂	EE 40 days	Dentate Gyrus	IHC	PV cell density	no change	[153] Serra et al. (2020)
Rat (Wistar)	Juvenile	Adult	♂	Exercise 40 days	Dentate Gyrus	IHC	PV cell density	increased	[153] Serra et al. (2020)
Rat (Sprague-Dawley)	Adolescent	Adolescent	♂	R- or S-ketamine 10mg/kg IP; sacrifice 30 mins later	Dentate Gyrus	IHC	PV cell density	decreased by S-ketamine	[185] Yang et al. (2015)

Rat (Sprague-Dawley)	Early postnatal	Juvenile; adult	♂	Oral FLX 10mg/kg/d from P2-P21	Dentate Gyrus	IHC; WFA stain	Total PV cell number; PNN+ fraction of PV cells	no change	[113] Mukhopadhyay et al. (2020)
Mouse (C57/BL6)	Prenatal, early postnatal	Early postnatal; juvenile	♂♀	Mothers given oral FLX 11.3mg/kg/d from GD7-P7	Dentate Gyrus	IHC; WHA stain	Total PV cell number; PV+/PNN+ cell number; PV intensity in PV+/PNN+ cells	no change	[171] Umemori et al. (2015)
PV-TRAP Mouse (C57/BL6)	Adult	Adult	♂♀	18 days oral FLX 0.167mg/ml in 1% saccharine drinking water	Dentate Gyrus	Electrophysiology	5HT-induced change in PV cell membrane potential	decreased (hyperpolarized)	[145] Sagi et al. (2020)
PV-TRAP Mouse (C57/BL6)	Adult	Adult	♂♀	18 days oral FLX 0.167mg/ml in 1% saccharine drinking water; 5HT5A receptor antagonist administered	Dentate Gyrus	Electrophysiology	5HT-induced change in PV cell membrane potential	no change	[145] Sagi et al. (2020)
PV-Cre Mouse (C57/BL6)	Adult	Adult	♂♀	18 days oral FLX 0.167mg/ml in 1% saccharine drinking water; PV cell-specific 5HT5A receptor KO	Dentate Gyrus	Electrophysiology	5HT-induced change in PV cell membrane potential	no change	[145] Sagi et al. (2020)
PV-TRAP Mouse (C57/BL6)	Adult	Adult	♂♀	18 days oral FLX 0.167mg/ml in 1% saccharine drinking water	Dentate Gyrus	Electrophysiology	5HT-induced PV cell firing frequency	decreased	[145] Sagi et al. (2020)
PV-Cre Mouse (C57/BL6)	Adult	Adult	♂♀	18 days oral FLX 0.167mg/ml in 1% saccharine drinking water; PV cell-specific 5HT5A receptor KO	Dentate Gyrus	Electrophysiology	5HT-induced PV cell firing frequency	no change	[145] Sagi et al. (2020)
PV-TRAP Mouse (C57/BL6)	Adult	Adult	♂♀	18 days oral FLX 0.167mg/ml in 1% saccharine drinking water	Dentate Gyrus	Electrophysiology	5HT-induced PV cell Kv channel potassium current amplitude	decreased	[145] Sagi et al. (2020)
PV-Cre Mouse (C57/BL6)	Adult	Adult	♂♀	18 days oral FLX 0.167mg/ml in 1% saccharine drinking water; PV cell-specific 5HT5A receptor KO	Dentate Gyrus	Electrophysiology	5HT-induced PV cell Kv channel potassium current amplitude	no change	[145] Sagi et al. (2020)
PV-TRAP Mouse (C57/BL6)	Adult	Adult	♂♀	18 days oral FLX 0.167mg/ml in 1% saccharine drinking water	Dentate Gyrus	Electrophysiology	Change in PV cell Kv channel potassium maximum current amplitude after 200nM PMA or 200nM PMA+30uM 5HT bath	decreased in FLX-treated but not vehicle-treated mice	[145] Sagi et al. (2020)
Tree Shrew (Tupaia Belangeri)	Adult	Adult	♂	5 weeks' daily psychosocial conflict; FLX (15mg/kg/day) or SLV-323 (20mg/kg/day) oral treatment daily for latter 4 weeks	CA1	IHC	Total PV cell number	no change	[30] Czeh et al. (2005)

Rat (Wistar)	Adolescent-adult	Adult	♂	FLX 15mg/kg/day or CLZ 20mg/kg/day with SI for 3 weeks	CA1	IHC	Total PV cell number	increased by FLX vs vehicle; decreased by FLX+SI, CLZ, and CLZ+SI vs vehicle; decreased by FLX+SI vs FLX	[43] Filipovic et al. (2017)
Rat (Wistar)	Juvenile-adolescent	Adult	♂	Physical exercise 40 days	CA1	IHC	Total PV cell number	increased	[57] Gomes da Silva et al. (2010)
Rat (Long-Evans)	Adult	Adult	♂	Physical exercise 30 min/day for 5 weeks	CA1	IHC	Total PV cell number	increased	[120] Nguyen et al. (2013)
Rat (Wistar)	Adult	Adult	♂	SI 6 weeks with anhedonic rats given tianeptine 10mg/kg/day IP for last 3 weeks	CA1	IHC	Total PV cell number	increased by tianeptine and tianeptine + SI vs their vehicle controls	[135] Peric et al. (2018)
Rat (Wistar)	Adult	Adult	♂	EE 2 months	CA1	IHC	Total PV cell number	no change	[148] Sampedro-Piquero et al. (2016)
Rat (Wistar)	Juvenile	Adult	♂	EE 40 days	CA1	IHC	PV cell density	no change	[153] Serra et al. (2020)
Rat (Wistar)	Juvenile	Adult	♂	Exercise 40 days	CA1	IHC	PV cell density	no change	[153] Serra et al. (2020)
Rat (Sprague-Dawley)	Adolescent	Adolescent	♂	R- or S-ketamine 10mg/kg IP; sacrifice 30 mins later	CA1	IHC	PV cell density	no change	[185] Yang et al. (2015)
Mouse (GAD-GFP)	Adult	Adult	♂	IP injection of 20mg/kg FLX daily for 2 weeks	CA1	IHC; WFA stain	Total PV cell number; total PV+/PNN+ cell number; PV+ fraction of PNN+ cells	decreased (all)	[62] Guirado et al. (2014)
Mouse (C57/BL6)	Adult	Adult	♂	10mg/kg/d oral FLX 30 days	CA1	IHC; WFA stain	PV+ fraction of PNN+ cells	decreased	[76] Karpova et al. (2014)
Rat (Sprague-Dawley)	Early postnatal	Juvenile; adult	♂	Oral FLX 10mg/kg/d from P2-P21	CA1	IHC; WFA stain	PNN+ fraction of PV cells; total PV cell number	decreased fraction in juveniles	[113] Mukhopadhyay et al. (2020)
Mouse (C57/BL6)	Prenatal, early postnatal	Early postnatal; juvenile	♂♀	Mothers given oral FLX 11.3mg/kg/d from GD7-P7	CA1	IHC; WHA stain	Total PV cell number; PV+/PNN+ cell number; PV intensity in PV+/PNN+ cells	no change	[171] Umemori et al. (2015)
Rat (Wistar)	Juvenile-adult	Adult	♂	8 weeks SI starting at P21, followed by 3 weeks re-isolation or pair housing and oral FLX 6mg/kg/d or vehicle	CA1	IHC	PV+/PNN+ cell number	decreased by FLX overall (net effect of re-isolates and pair housing groups combined)	[109] Mikics et al. (2018)

Mouse (C57/BL6)	Adult	Adult	♂	Isoflurane anaesthesia 30 mins	CA1	IHC	FosB intensity in PV+ cells	increased	[5] Antila et al. (2017)
Tree Shrew (Tupaia Belangeri)	Adult	Adult	♂	5 weeks' daily psychosocial conflict; FLX (15mg/kg/day) or SLV-323 (20mg/kg/day) oral treatment daily for latter 4 weeks	CA2	IHC	Total PV cell number	Decreased by stress; rescued by SLV-323	[30] Czeh et al. (2005)
Rat (Wistar)	Adolescent-adult	Adult	♂	FLX 15mg/kg/day or CLZ 20mg/kg/day with SI for 3 weeks	CA2	IHC	Total PV cell number	increased by FLX + SI and CLZ + SI vs SI alone	[43] Filipovic et al. (2017)
Rat (Wistar)	Adult	Adult	♂	SI 6 weeks with anhedonic rats given tianeptine 10mg/kg/day IP for last 3 weeks	CA2	IHC	Total PV cell number	increased by tianeptine and tianeptine + SI vs their vehicle controls	[135] Peric et al. (2018)
Rat (Wistar)	Juvenile-adolescent	Adult	♂	Physical exercise 40 days	CA2/3	IHC	Total PV cell number	increased	[57] Gomes da Silva et al. (2010)
Rat (Long-Evans)	Adult	Adult	♂	Physical exercise 30 min/day for 5 weeks	CA2/3	IHC	Total PV cell number	increased	[120] Nguyen et al. (2013)
Rat (Wistar)	Juvenile	Adult	♂	EE 40 days	CA2/3	IHC	PV cell density	no change	[153] Serra et al. (2020)
Rat (Wistar)	Juvenile	Adult	♂	Exercise 40 days	CA2/3	IHC	PV cell density	increased	[153] Serra et al. (2020)
Tree Shrew (Tupaia Belangeri)	Adult	Adult	♂	5 weeks' daily psychosocial conflict; FLX (15mg/kg/day) or SLV-323 (20mg/kg/day) oral treatment daily for latter 4 weeks	CA3	IHC	Total PV cell number	Decreased by stress; rescued by SLV-323	[30] Czeh et al. (2005)
PV-Cre mice	Adult	Adult	♂	EE	Dorsal CA3b	IHC	Total PV cell number	no change	[35] Donato et al. (2013)
Rat (Wistar)	Adolescent-adult	Adult	♂	FLX 15mg/kg/day or CLZ 20mg/kg/day with SI for 3 weeks	CA3	IHC	Total PV cell number	increased by FLX + SI and CLZ + SI vs SI alone	[43] Filipovic et al. (2017)
Mouse (C57/BL6)	Adult	Adult	♂	FLX 10mg/kg/day SC for 21 days starting at P90	CA3	IHC	Total PV cell number	no change	[55] Godavarthi et al. (2014)
Rat (Wistar)	Adult	Adult	♂	SI 6 weeks with anhedonic rats given tianeptine 10mg/kg/day IP for last 3 weeks	CA3	IHC	Total PV cell number	increased by tianeptine and tianeptine + SI vs their vehicle controls	[135] Peric et al. (2018)

Rat (Wistar)	Adult	Adult	♂	EE 2 months	CA3	IHC	Total PV cell number	no change	[148] Sampedro-Piquero et al. (2016)
Rat (Sprague-Dawley)	Adolescent	Adolescent	♂	R- or S-ketamine 10mg/kg IP; sacrifice 30 mins later	CA3	IHC	PV cell density	no change	[185] Yang et al. (2015)
Rat (Sprague-Dawley)	Early postnatal	Juvenile; adult	♂	Oral FLX 10mg/kg/d from P2-P21	CA3	IHC; WFA stain	Total PV cell number; PNN+ fraction of PV cells	decreased fraction in juveniles	[113] Mukhopadhyay et al. (2020)
Mouse (C57/BL6)	Adult	Adult	♂	FLX 15mg/kg/day IP for 3 weeks	CA3	IHC; WFA stain	PV cell density; PV+/PNN+ cell density; PNN+ fraction of PV cells	decreased PV cell density and PV+/PNN+ cell density	[124] Ohira et al. (2013)
PV-Cre mice	Adult	Adult	♂	EE	Dorsal CA3b	IHC	fraction of PV cells expressing low amounts of PV	increased in basket cells and PV cells overall (not chandelier cells)	[35] Donato et al. (2013)
PV-Cre mice	Adult	Adult	♂	EE	Dorsal CA3b	IHC	Inhibitory puncta densities onto PV dendrites	increased	[35] Donato et al. (2013)
PV-Cre mice	Adult	Adult	♂	EE	Dorsal CA3b	Chemogenetic activation of PV cells; IHC	fraction of PV cells expressing high amounts of PV	increased	[35] Donato et al. (2013)
Rat (Wistar)	Juvenile	Adult	♂	EE 40 days	Subiculum	IHC	PV cell density	no change	[153] Serra et al. (2020)
Rat (Wistar)	Juvenile	Adult	♂	Exercise 40 days	Subiculum	IHC	PV cell density	increased	[153] Serra et al. (2020)
Rat (Wistar)	Juvenile	Adult	♂	EE 40 days	Hilus	IHC	PV cell density	no change	[153] Serra et al. (2020)
Rat (Wistar)	Juvenile	Adult	♂	Exercise 40 days	Hilus	IHC	PV cell density	no change	[153] Serra et al. (2020)
PV-TRAP Mouse (C57/BL6)	Adult	Adult	♂♀	18 days oral FLX 0.167mg/ml in 1% saccharine drinking water	Subgranular zone	IHC	5HT5A+ fraction of PV cells	no change	[145] Sagi et al. (2020)
PV-TRAP Mouse (C57/BL6)	Adult	Adult	♂♀	18 days oral FLX 0.167mg/ml in 1% saccharine drinking water	Subgranular zone	IHC	pKv3.1b+ fraction of PV cells	increased	[145] Sagi et al. (2020)
PV-Cre Mouse (C57/BL6)	Adult	Adult	♂♀	18 days oral FLX 0.167mg/ml in 1% saccharine drinking water; PV cell-specific 5HT5A receptor KO	Subgranular zone	IHC	pKv3.1b+ fraction of PV cells	no change	[145] Sagi et al. (2020)

Mouse (C57/BL6)	Adolescent-adult	Adult	♂	Dried bonito broth (10%) intake 53 days	Hippocampus	IHC	PV cell density	increased	[73] Jargalsaikhan et al. (2016)
Mouse (GAD-GFP)	Adult	Adult	♂	IP injection of 20mg/kg FLX daily for 2 weeks	Hippocampus	IHC; WFA stain	Total PV cell number; total PV+/PNN+ cell number; PV+ fraction of PNN+ cells; perisomatic PV and synaptophysin puncta densities on pyramidal cells	decreased PV+/PNN+ cell number and PV+ fraction of PNN+ cells	[62] Guirado et al. (2014)
Rat (Wistar)	Juvenile	Adult	♂	EE 40 days	Hippocampus	IHC; Western blot	PV cell density; PV protein content	no change	[153] Serra et al. (2020)
Rat (Wistar)	Juvenile	Adult	♂	Exercise 40 days	Hippocampus	IHC; Western blot	PV cell density; PV protein content	increased protein and density	[153] Serra et al. (2020)
Rat (Wistar)	Juvenile-adolescent	Adult	♂	Physical exercise 40 days	Hippocampus	Western blot	PV protein content	increased	[57] Gomes da Silva et al. (2010)
Rat (Sprague-Dawley)	Adolescent-adult	Adult	♂	Paroxetine 5mg/kg/day injection for 12 days	Hippocampus	2D gel then mass spectrometry proteomics on hippocampus samples	PV protein content	decreased 1.3-fold	[104] McHugh et al. (2009)
Rat (Sprague-Dawley)	Adult	Adult	♂	IFS 15 mins on day 0, then EE 2h/day for 30 days. Brains collected on day 46	Hippocampus	Western blot	PV protein content	IFS reduced PV protein, EE + IFS rescued normal amount. No change for EE alone	[163] Sun et al. (2016)
Rat (Wistar)	Adult	Adult	♂	Neuregulin-1 infusion to lateral ventricles same time as ketamine 10mg/kg IP	Hippocampus	Western blot	PV protein content	decreased by ketamine but not ketamine + neuregulin-1	[176] Wang et al. (2014)
Rat (Wistar-Kyoto)	Adolescent	Adolescent	♂	7h/day exposure to roman chamomile essential oil or a-pinene vapors for 14 days	Hippocampus	qPCR	PV mRNA expression	increased by roman chamomile and a-pinene	[83] Kong et al. (2017)
PV-TRAP Mouse (C57/BL6)	Adult	Adult	♂♀	18 days oral FLX 0.167mg/ml in 1% saccharine drinking water	Hippocampus	Translating ribosome affinity purification (TRAP)	PV cell 5HT5A receptor mRNA	no change	[145] Sagi et al. (2020)
PV-TRAP Mouse (C57/BL6)	Adult	Adult	♂♀	18 days oral FLX 0.167mg/ml in 1% saccharine drinking water	Hippocampus	Western blot	5HT5A receptor protein level in membrane-bound fraction of hippocampal lysate	increased	[145] Sagi et al. (2020)
Rat (Wistar)	Adult	Adult	♂	SI 6 weeks with anhedonic rats given tianeptine 10mg/kg/day IP for last 3 weeks	Dorsal Hippocampus	IHC	Total PV cell number	increased by tianeptine and tianeptine + SI vs their vehicle controls	[135] Peric et al. (2018)

Rat (Wistar)	Adult	Adult	♂	Lurasidone 3mg/kg/day oral for 5 weeks	Dorsal Hippocampus	qPCR; Western blot	PV mRNA expression; PV protein content	decreased mRNA	[144] Rossetti et al. (2018)
Rat (Wistar)	Adult	Adult	♂	CMS 2 weeks, then anhedonic rats received 5 more weeks CMS + lurasidone 3mg/kg/day oral	Dorsal Hippocampus	qPCR; Western blot	PV mRNA expression; PV protein content	no change	[144] Rossetti et al. (2018)
Rat (Wistar)	Adult	Adult	♂	Lurasidone 3mg/kg/day oral for 5 weeks	Ventral Hippocampus	qPCR; Western blot	PV mRNA expression; PV protein content	no change	[144] Rossetti et al. (2018)
Rat (Wistar)	Adult	Adult	♂	CMS 2 weeks, then anhedonic rats received 5 more weeks CMS + lurasidone 3mg/kg/day oral	Ventral Hippocampus	qPCR; Western blot	PV mRNA expression; PV protein content	no change	[144] Rossetti et al. (2018)
Sprague-Dawley rats	Adult	Adult	♂	Daily FS P65-P74, RS 1hr on P65, P66, P74; VPA IP 300mg/kg or vehicle P60-74	Ventral Hippocampus	IHC	Total PV cell number	decreased by VPA and VPA + stress at 12 weeks old; decreased by VPA + stress at 16 weeks old	[56] Gomes et al. (2019)
Sprague-Dawley rats	Adult	Adult	♂	Daily FS P65-P74, RS 1hr on P65, P66, P74; VPA IP 300mg/kg or vehicle P60-74	Ventral Hippocampus	IHC and WFA stain	Total PV/PNN+ cell number	decreased by VPA and VPA + stress at 12 weeks old; decreased by VPA + stress at 16 weeks old	[56] Gomes et al. (2019)
Mouse (C57/BL6)	Adult	Adult	♂	FLX 10mg/kg/day SC 24 days	Basolateral Amygdala	IHC	Total PV cell number	no change	[55] Godavarthi et al. (2014)
Mouse (C57/BL6)	Adolescent-adult	Adult	♂	Dried bonito broth (10%) intake 53 days	Basolateral Amygdala	IHC	PV cell density	increased	[73] Jargalsaikhan et al. (2016)
Rat (Wistar)	Adult	Adult	♂	EE 2 months	Basolateral Amygdala	IHC	Total PV cell number	no change	[148] Sampedro-Piquero et al. (2016)
Rat (Wistar)	Adolescent	Adult	♂	EE 35 days	Basolateral Amygdala	IHC	Total PV cell number; large and small PV cell number	increased total and small PV cell number	[172] Urakawa et al. (2013)
Mouse (C57/BL6)	Prenatal, early postnatal	Early postnatal; juvenile	♂♀	Mothers given oral FLX 11.3mg/kg/d from GD7-P7	Basolateral Amygdala	IHC; WFA stain	Total PV cell number; PV+/PNN+ cell number; PV intensity in PV+/PNN+ cells	decreased PV+/PNN+ cell number at P17 but not P24; other measures unchanged	[171] Umemori et al. (2015)
Mouse (C57/BL6)	Adult	Adult	♂	10mg/kg/d oral FLX 30 days	Basolateral Amygdala	IHC; WFA stain	PV+ fraction of PNN+ cells	decreased	[76] Karpova et al. (2014)

Rat (Sprague-Dawley)	Juvenile	Adolescent	♀	1 week EE	Basolateral Amygdala	IHC; WFA stain	c-Fos+ proportion of PV cells; WFA+ proportion of PV cells; c-Fos+ proportion of WFA+ PV cells	decreased c-Fos+ proportion of PV cells; decreased c-Fos+ proportion of WFA+ PV cells	[174] Vazquez-Sanroman et al. (2020)
Rat (Sprague-Dawley)	Early postnatal; adolescent	Adolescent	♀	MS 4h/day from P2-P20; treatment with COX-2 inhibitor NS-398 (8mg/kg) every other day IP from P30-P38; LH task P41	Basolateral Amygdala	Western blot	PV protein content	no change	[96] Lukkes et al. (2017)
Rat (Sprague-Dawley)	Early postnatal; adolescent	Adolescent	♀	MS 4h/day from P2-P20; treatment with COX-2 inhibitor NS-398 (8mg/kg) every other day IP from P30-P38; LH task P41; allowed to witness another rat in task 1d before they did it.	Basolateral Amygdala	Western blot	PV protein content	no change	[96] Lukkes et al. (2017)
Rat (Wistar)	Adolescent	Adult	♂	EE 35 days	Lateral Amygdala	IHC	Large and small PV cell number	no change	[172] Urakawa et al. (2013)
Rat (Sprague-Dawley)	Adolescent	Adolescent	♂	R- or S-ketamine 10mg/kg IP; sacrifice 30 mins later	Nucleus Accumbens	IHC	PV cell density	no change	[185] Yang et al. (2015)
Rat (Wistar)	Juvenile-adult	Adult	♂♀	SI + 7 weeks with or without 5mg/kg/day oral apocynin	Nucleus Accumbens	IHC	PV immunoreactivity	decreased by SI alone, no change in apocynin alone or SI + apocynin	[150] Schiavone et al. (2009)
Rat (Wistar)	Juvenile-adult	Adult	♂♀	SI + 7 weeks with or without 5mg/kg/day oral apocynin	Nucleus Accumbens	Western blot	PV protein content	decreased by SI alone, no change in apocynin alone or SI + apocynin	[150] Schiavone et al. (2009)
Mouse (C57/BL6)	Adolescent	Adolescent	♂♀	EE or EE + RS 2h/d for 7 days	Barrel cortex	IHC	c-Fos+ fraction of PV cells	increased in both	[23] Chen et al. (2018)
Mouse (C57/BL6)	Early postnatal	Early postnatal, adult	♂♀	EE from late pregnancy until P21	Lateral Striatum	IHC and WFA stain	High-PV and low-PV cell density; high-PV and low-PV PNN+ cell density	increased low-PV cell density and low-PV/PNN+ cell density in early postnatal and adult mice	[123] O'Connor et al. (2019)
Mouse (C57/BL6)	Early postnatal	Early postnatal, adult	♂♀	EE from late pregnancy until P21	Medial Striatum	IHC and WFA stain	High-PV and low-PV cell density; high-PV and low-PV PNN+ cell density	increased low-PV cell density and low-PV/PNN+ cell density in adults	[123] O'Connor et al. (2019)
Rat (Sprague-Dawley)	Early postnatal; adolescent	Adolescent	♀	MS 4h/day from P2-P20; treatment with COX-2 inhibitor NS-398 (8mg/kg) every other	Dorsal Raphe Nucleus	Western blot	PV protein content	increased	[96] Lukkes et al. (2017)

				day IP from P30-P38; LH task P41					
Rat (Sprague-Dawley)	Early postnatal; adolescent	Adolescent	♀	MS 4h/day from P2-P20; treatment with COX-2 inhibitor NS-398 (8mg/kg) every other day IP from P30-P38; LH P41; allowed to witness another rat in task 1 day before they did it.	Dorsal Raphe Nucleus	Western blot	PV protein content	no change	[96] Lukkes et al. (2017)
Mouse (C57/BL6)	Adult	Adult	♂	FLX 15mg/kg/day IP 3 weeks	Thalamic Reticular Nucleus	IHC and WFA stain	PV cell density; PV+/PNN+ cell density; PNN+ fraction of PV cells	no change	[124] Ohira et al. (2013)
Mouse (C57/BL6)	Adolescent-adult	Adult	♂	Dried bonito broth (10%) intake 53 days	Superior Colliculus	IHC	PV cell density	increased	[73] Jargalsaikhan et al. (2016)
Mouse (C57/BL6)	Adult	Adult	♂	CSD 10 days followed by 20mg/kg/day FLX IP or vehicle for 14 days	Ventral Pallidum	Electrophysiology	Number of spikes elicited by 100pA current injection in PV(VP-->LHb) cells; ratio of excitatory:inhibitory inputs onto PV(VP-->LHb) cells	CSD alone increased number of spikes in resilient and susceptible mice, prevented by FLX; decreased ratio in resilient and FLX-treated mice compared to susceptible	[82] Knowl et al. (2017)
Mouse (C57/BL6)	Adult	Adult	♂	CSD 10 days followed by 20mg/kg/day FLX IP or vehicle for 14 days	Ventral Pallidum	Electrophysiology	Number of spikes elicited by 100pA current injection in PV(VP-->VTA) cells; ratio of excitatory:inhibitory inputs onto PV(VP-->VTA) cells	decreased spike number in resilient and FLX (FLX vs. susceptible only) mice but not susceptible; ratio increased in susceptible mice	[82] Knowl et al. (2017)

Mouse and rat life stages were defined as the following: early postnatal: P0-19 (postnatal day 0-19, where day of birth is P0; juvenile: P20-30; adolescent: P31-60; and adult: P61+. Abbreviations: CLZ: clozapine; CNO: clozapine N-oxide; CMS: chronic mild stress; CNO: clozapine N-oxide; CSD: chronic social defeat; CSPG: chondroitin sulfate proteoglycan; CUS: chronic unpredictable stress; DREADD: designer receptor exclusively activated by designer drugs; EE: environmental enrichment; FLX: fluoxetine; IFS: inescapable foot shocks; IHC: immunohistochemistry; IL-10: interleukin-10; IP: intraperitoneal; LHb: lateral habenula; mRNA: messenger ribonucleic acid; MS: maternal separation; qPCR: quantitative polymerase chain reaction; RS: restraint stress; SI: social isolation; SC: subcutaneous; VP: ventral pallidum; VPA: valproic acid; VTA: ventral tegmental area; WFA: Wisteria floribunda agglutinin.

Table 5: PV neuron alterations in post-mortem samples from patients having died with mood disorders

Sex	Disorder	Brain region	Method	Measure	Outcome	Reference
5M, 6F	MDD	Dorsolateral Prefrontal Cortex	IHC; WFA stain	PV cell density; PNN+ fraction of PV cells; PV+ fraction of PNNs	no change	[1] Alcaide et al. (2019)
9M, 6F	MDD	Dorsolateral Prefrontal Cortex	IHC	PV cell density	no change	[9] Beasley et al. (2002)
4M, 7F	MDD	Dorsolateral Prefrontal Cortex layers 2-6	IHC	PV stain intensity	decreased in layer 6, no change in other layers	[78] Khundakar et al. (2010)
22M, 18F	MDD	Right Dorsolateral Prefrontal Cortex	qPCR	PV mRNA expression	decreased	[26] Chung et al. (2018)
10M, 9F	MDD	Dorsolateral Prefrontal Cortex	qPCR	PV mRNA expression	no change	[156] Sibille et al. (2012)
8M, 6F	MDD	Orbitofrontal Cortex, Dorsolateral Prefrontal Cortex	IHC	PV cell density	decreased in Orbitofrontal Cortex	[140] Rajkowska et al. (2007)
9M, 6F	MDD	Brodman Area 24	IHC	PV cell density in different layers; PV cell clustering	no change	[28] Cotter et al. (2002)
matched with control	MDD	CA1, CA2, CA3, CA4, Entorhinal Cortex, Subiculum	IHC	Total PV cell number; PV cell density	no change	[81] Knable et al. (2004)
9M, 8F	MDD	Tpt Auditory Association Cortex	IHC	PV cell size; PV cell density	no change	[157] Smiley et al. (2016)
9M	DS-CA	Ventromedial Prefrontal Cortex	IHC, WFL stain	PNN+ fraction of PV cells	increased vs depressed-suicide and controls	[165] Tanti et al. (2020)
26M, 25F	MDD	Subgenual Anterior Cingulate Cortex, Amygdala	qPCR	PV mRNA expression	decreased in subgenual anterior cingulate	[167] Tripp et al. (2012)
5M, 8F	BD	Dorsolateral Prefrontal Cortex	IHC; WFA stain	PV cell density; PNN+ fraction of PV cells; PV+ fraction of PNNs	no change	[1] Alcaide et al. (2019)
9M, 6F	BD	Dorsolateral Prefrontal Cortex	IHC	PV cell density	no change	[9] Beasley et al. (2002)
1M, 4F	BD	Brodman Area 9	IHC	PV cell density	no change	[146] Sakai et al. (2008)
8M, 10F	BD	Brodman Area 9 layers 2-6	ISH	Total PV cell number; PV+/NR2A+ cell density; NR2A density in PV cells	no change	[13] Bitanirwe et al. (2010)

22M, 18F	BD	Right Dorsolateral Prefrontal Cortex	qPCR	PV mRNA expression	decreased	[26] Chung et al. (2018)
10M, 9F	BD	Dorsolateral Prefrontal Cortex	qPCR	PV mRNA expression	decreased, but unchanged after exclusion of subject pairs with potential confounding factors	[156] Sibille et al. (2012)
20M/15F	Low GABA marker BD*	Brodmann Area 9 grey matter	qPCR	PV mRNA expression	decreased vs controls and non-low GABA marker subjects	[175] Volk et al. (2016)
20M/15F	Non-low GABA marker BD*	Brodmann Area 9 grey matter	qPCR	PV mRNA expression	decreased vs controls	[175] Volk et al. (2016)
matched with control	BD	Lateral, Basal, Accessory Basal, and Cortical Nuclei of the Amygdala	IHC	PV cell density	66% decrease in Lateral Nucleus	[11] Berretta et al. (2003)
7M, 4F	BD	Lateral, Basal, Accessory Basal, and Cortical Nuclei of the Amygdala	IHC	PV cell density; Total PV cell number	no change	[134] Pantazopoulos et al. (2010)
9M, 6F	BD	Brodmann Area 24	IHC	PV cell density in different layers; PV cell clustering	increased clustering	[28] Cotter et al. (2002)
matched with control	BD	CA1, CA2, CA3, CA4, Entorhinal Cortex, Subiculum	IHC	Total PV cell number; PV cell density	decreased PV cell number in CA2	[81] Knable et al. (2004)
5M, 9F	BD	CA1, CA2/3, and CA4	IHC	Total PV cell number	decreased in CA1 and CA4	[84] Konradi et al. (2011)
6M, 4F	BD	Entorhinal Cortex	IHC	PV soma size; Total PV cell number; PV cell density	decreased PV cell number and density	[133] Pantazopoulos et al. (2007)
4M, 9F	BD	Parasubiculum; Deep Entorhinal Cortex; Total Entorhinal Cortex	IHC	PV cell density	decreased	[177] Wang et al. (2011)
4M, 9F	BD	Superficial Entorhinal Cortex; Subiculum; Pre-subiculum	IHC	PV cell density	no change	[177] Wang et al. (2011)
9M, 6F	BD	Thalamic Reticular Nucleus	IHC	Total PV cell number	decreased	[162] Steullet et al. (2018)

All studies were conducted with samples from adults, with a mean age ≥ 35 years. Abbreviations: BD: bipolar disorder; DS-CA: depressed-suicide + child abuse history; GABA: gamma-amino butyric acid; IHC: immunohistochemistry; ISH: in situ hybridization; MDD: major depressive disorder; qPCR: quantitative polymerase chain reaction. *Low GABA marker and non-low GABA marker BD subjects were divided by quantifying GAD67, PV, SST, and Lxh6 mRNA.