INTRODUCTION

S100 is a group of proteins that part calcium-binding protein family (Xia et al., 2018), with evidence of participation in several intracellular and extracellular regulatory activities, following the example of S100B and S100A10 proteins (Donato, 2003). Besides their important physiological functions, such as cell differentiation and calcium homeostasis, their expressions also have evident correlations with pathological processes, such inflammation and neoplasia. (Allgöwer et al., 2020; Gonzalez et al., 2020; Quilaqueo et al., 2021).

From this perspective, S100 has gained prominence in terms of its expression in different brain structures, such as the thalamus, located in diencephalon, which actively transmits and regulates information to cerebral cortex. In recent decades, studies have increasingly emphasized the importance of thalamic nuclei in modulating and processing stimuli from sensory pathways to the cortex in a mutual activation, in addition their participation in somatosensory, behavioral, memory and cognitive circuits in general (Saalmann & Kastner, 2015). In this context, thalamic tagging with S100 proteins has shown promising results, which allow relating the presence of these protein events of various natures, encompassing also mental disorders (Zhang et al., 2011; Bean et al., 2014).

In this prism, there is a clear need for a better understanding of these proteins due their significant implications, both physiological and pathological, in Central Nervous System, especially in order to elucidate their role in clinical and pre-clinical conditions (Arrais et al., 2022). Given the relevance of this theme, this study aimed to discuss the relationships between S100 proteins and the thalamus.
MATERIAL AND METHOD

This study is an integrative literature review, using the Pubmed database, and following the MeSH terms: S100 and Thalamus. The terms were searched together, and the time period analyzed was the last decade. In total, the search returned 32 results. Studies returned by the Pubmed search, using Boolean operators, for "S100 AND Thalamus" published from 2011 to October 2022 were included in the review. Articles that did not discuss S100 or Thalamus, as well as those that addressed these topics in a dissociated or secondary manner were excluded. Of the 32 articles, 18 were excluded for not addressing the topic, and then 2 more were excluded for not addressing the central research question. Finally, 12 studies were used.

RESULTS AND DISCUSSION

The data extracted are shown in Table I.

The data found in the literature showed several relationships between S100 proteins and thalamus level lesion, such as neoplasms. These proteins were seen through immunoreactivity in an extraventricular atypical thalamic neurocytoma, expressed together with synaptophysin, beta-chainin and CD56 (Rusiecki et al., 2017). Besides this, there is also a report of granular cell astrocytoma in which the imaging exam (nuclear magnetic resonance) showed lesion in bilateral anterior temporal lobe, left parietal lobe, left thalamus and cerebellum, where showed immunopositivity for S100 (Dutta et al., 2020). Furthermore, there was a case of primary pineal malignant melanoma with diffuse tumor infiltration to pulvinar, posterior thalamus, and colliculi, positive for S100 reactive protein, being understood with sensitivity 89 % and specificity 70 - 77 % for melanomas (Wendel et al., 2018).

Additionally to neoplasms, the presence S100 in the thalamus has been related to mental disorders. In one of the

![Fig. 1. S100 protein dimer structure Heizmann 2002.](image1)

![Fig. 2. Flowchart of article selection.](image2)

Table I. List of studies included in review.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Objective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aridas et al.</td>
<td>2014</td>
<td>Correlate physiological, biochemical, radiological and histological markers of neuronal cell degeneration after induction neonatal hypoxic-ischemic encephalopathy in animal model (lambs).</td>
</tr>
<tr>
<td>Bartkowska et al.</td>
<td>2017</td>
<td>Characterize effect of stress on S100A6 in brain structures and identify phenotype of cells populations that express S100A6 in response to unpredictable chronic stress.</td>
</tr>
<tr>
<td>Bean et al.</td>
<td>2014</td>
<td>Identify neurons or cells where ErbB4 protein expressed in the brain.</td>
</tr>
<tr>
<td>Chang et al.</td>
<td>2012</td>
<td>Evaluate prognostic value of HSP70, S100B, NSE and plasma levels of nuclear and mitochondrial DNA in temporal lobe epilepsy.</td>
</tr>
<tr>
<td>Dutta et al.</td>
<td>2020</td>
<td>Descriptive case of a man 50 year old whose diagnosis of granular cell astrocytoma was a dilemma due to its radiological and histopathological features.</td>
</tr>
<tr>
<td>Haligur et al.</td>
<td>2019</td>
<td>Investigate pathogenesis of listeria encephalitis using GFAP, S100 protein, NMDAR1 and ICOS.</td>
</tr>
<tr>
<td>Kadar et al.</td>
<td>2011</td>
<td>Investigate gene expression profile during high-frequency stimulation (HFS) of ventrolateral thalamic nucleus.</td>
</tr>
<tr>
<td>Muneoka et al.</td>
<td>2012</td>
<td>Analyze the glia of ventroposterior thalamus and habenula using immunohistochemistry.</td>
</tr>
<tr>
<td>Rusiecki et al.</td>
<td>2017</td>
<td>Case report of pathologic and molecular findings of an extraventricular neurocytoma that evolutted to an anaplastic ganglioma.</td>
</tr>
<tr>
<td>Wendel et al.</td>
<td>2018</td>
<td>Case report of a man 53 year old with primary melanoma in the pienceal region.</td>
</tr>
<tr>
<td>Zhang et al.</td>
<td>2011</td>
<td>Investigate hypothesis that levels of p11 mRNA (S100A10) in peripheral blood may serve as an adjuvant biomarker of bipolar disorder and correlate with neural activity.</td>
</tr>
</tbody>
</table>

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studies, S100B expression was evidenced through immunohistochemistry in the ventro-posterior nucleus of the thalamus and in the habenula, areas that are related to mental disorders, where the investigation of the protein may be the key to a better understanding of pathological processes existing in these areas (Muneokka et al., 2012). More specifically, regarding bipolar disorder, decreased glucose metabolism has been found at the thalamic level, while S100A10 expression is up-regulated at the blood level (Zhang et al., 2011). A study with schizophrenia patients showed positivity for S100 in thalamic cells with the ErbB4 receptor - a known genetic risk factor for this pathology (Bean et al., 2014).

Another strong relationship is S100 proteins with hypoxia, trauma and stress in the central nervous system. A study with lambs, it was shown a marked neuropathology by asphyxia, causing thalamus neuronal degeneration and astrogliosis, with a five-fold elevation of brain concentration S100B (Aridas et al., 2014). In traumatic injuries to the brain, studied in rats, a modification was seen in the expression of 4964 genes in the perilesional cortex and 1966 genes in the thalamus 3 months after the event, and an increase in S100A4 gene expression was observed, where expression is linked to important post-traumatic events such as epileptogenesis and tissue repair (Lipponen et al., 2016). Another study addressed the association of S100A6 with stress, but that memora amount of the protein was found in the thalamus (Bartkowska et al., 2017).

In addition, three remaining studies address bacterial infection, Parkinson's disease, and epilepsy. In one of these studies, S100 protein expression in areas affected by listeria encephalitis, including the thalamus, provides clues about how bacterium affects the nervous system (Haligur et al., 2019). In temporal lobe epilepsy, there is a correlation between higher serum S100BP level, thalamic gray matter atrophy and affected cognitive process (Chang et al., 2012). In Parkinson's disease, high frequency stimulation (HFS) of ventrolateral thalamic nucleus, used for treatment residual tremor, is able modulate expression of 176 hippocampal genes, including those encoding S100A4 protein (Kádár et al., 2011).

CONCLUSION

S100 proteins are important markers of thalamic injury, especially in cases of neoplasia and mental disorders. Furthermore, these proteins are related to situations such as hypoxia, trauma, bacterial infections, Parkinson's disease, and epilepsy. In view of these findings, it is important to carry out further studies on their action in the Central Nervous System, focusing on the thalamus, in order to elucidate their significance in clinical and pre-clinical pictures and prognostic value.

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REFERENCES


