

Table S1: Lesion profiles in different brain regions of C-, H- and L-type BSE infected cattle (literature review)

BSE	Brainstem	Cerebellum	Midbrain	Diencephalon and Cerebrum*	Others brain regions	Remarks
C-type (field)	Brainstem: ++ ^[43] DMNV: +(+) ^[20] ; +++ ^[40,44,3] Nc. Sol. Trac., Nc. Trigem: +++ ^[11,16,18,19,17,20,40,44] Nc. Hyp.: (+) ^[16,18,19] ; + ^[20] Nc. Coch.: (+) ^[16,18,19] Vest. Compl.: + ^[16,18,19,20,40] ; ++ ^[17] ; +++ ^[3,40] Ret. Form, Olive: +++ ^[3,40] ; + ^[20,44]	Vermis: (+) ^[11,16,18,19,20,43] Medulla: + ^[43] Cortex: (+) ^[43]	Midbrain: ++ ^[43] Centr. Grey: +++ ^[40,11,16,17] ; +(+) ^[19] Rostr. Coll: ++ ^[16,18,19] Med. Gen. Nc: + ^[16,18,19] Nc. Ruber: +++ ^[3] ; + ^[20] Subst. Nigra: +(+) ^[20]	Tha.: + ^[41,16,18,19] ; +(+) ^[43] ; ++ ^[40] Hyp.: ++ ^[11,16,18,19] ; +++ ^[40] Hip.: (+) ^[43] ; ++ ^[11] Cortex: (+) ^[11,16,18,19] ; + ^[40,43] ; ++ ^[40]	CS: + ^[11] ; +(+) ^[43] Caud.: (+) ^[16,18,19] ; +++ ^[40] Put.: + ^[16,18,19] ; +++ ^[40] Sept.: (+) ^[16,18,19] ; + ^[11] Claustr.: Negative ^[16,18,19] OB: (+) ^[43] LoP: + ^[43]	Preclinical animals with mild lesions in Nc. Sol. Trac., Nc. Trigem., DMNV, Ret. Form. ^[41] Vest. Compl. affected in early disease ^[54] Two cows with a different lesion profile (Vermis, Tha, Cortex: B>A; MB: A>B) ^[40]
C-type (IC)	Nc. Sol. Trac., Nc. Trigem: +++ ^[28] Nc. Hyp.: (+) ^[28] Nc. Coch, Vest. Compl.: ++ ^[28]	Vermis: (+) ^[28]	Centr. Grey, Rostr. Coll., Med. Gen. Nc.: +++ ^[28]	Tha., Hyp.: +++ ^[28] Cortex: (+) ^[28]	Caud.: + ^[28] Put: +++ ^[28] Sept.: (+) ^[28] Claustr.: (+) ^[28]	Lesion profile comparable to natural infected BSE cases ^[28]
H-type (field)	Brainstem: + ^[23] Nc. Sol. Trac., Nc. Trigem: +++ ^[21] ; + ^[22] DMNV: less severe ^[21] Olive: +++ ^[21]	NA	Midbrian: + ^[23]	NA	NA	No amyloid in brainstem ^[22]
H-type (IC)	Brainstem: ++(+) ^[27] Nc. Sol. Trac., Nc. Trigem: +++ ^[26] Nc. Hyp.: + ^[26] Nc. Coch, Vest. Compl.: ++ ^[26]	Vermis: ++ ^[26] ; ++(+) ^[27]	Centr. Grey, Rostr. Coll.: +++ ^[26] Med. Gen. Nc.: ++(+) ^[26]	Tha.: ++(+) ^[27] ; +++ ^[26] Hyp.: +++ ^[26] Hip.: +++ ^[27] Cortex: ++ ^[25,26,30,31,29] ; ++(+) ^[27]	Caud.: ++ ^[26] Put.: ++ ^[26] Sept.: (+) ^[26] Claustr.: + ^[26] BG: ++(+) ^[27] LoP: +++ ^[27]	Brainstem with mildest lesions in pons and Nc. Hyp. ^[27] C-Type with no lesion in Vermis ^[26] , with less lesions in Cortex ^[30,31,26] , Caud. and Put ^[26] , but more lesions in Sept. ^[26]

L-type (field)	NA	NA	NA	<i>Tha.</i> : + ^[7] <i>Hip., Cortex</i> : negative ^[7]	NA	Brainstem lesions are not consistently seen ^[7]
	<i>Nc. Sol. Trac., Nc. Trigem.</i> : +++ ^[24,25,29]	<i>Vermis</i> : (+) ^[24] ; + ^[25,29]	<i>Centr. Grey, Rostr. Coll.</i> : +++ ^[25,24,29]	<i>Tha., Hyp</i> : ++ ^[24,25,29] <i>Cortex</i> : (+) ^[6] ; ++ ^[5,10,11,14]	<i>Caud.</i> : (+) ^[24] + ^[25,29] <i>Put.</i> : (+) ^[24] ; ++ ^[25,29]	C-type with less lesions in Cortex ^[30,31]
L-type (IC)	<i>Nc. Hyp.</i> : Negative ^[24] ; (+) ^[25,29] <i>Nc. Coch. Vest. Compl.</i> : (+) ^[24] ++ ^[25,29]		<i>Med. Gen. Nc.</i> : ++ ^[24] ; +++ ^[25,29]		<i>Sept., Claustr.</i> : (+) ^[24] ; + ^[25,29]	C-type with distinctly more lesion in Put. ^[24]
L-type (oral)	<i>Brainstem</i> : + ^[47] <i>DMNV</i> : negative ^[47]	<i>Cortex</i> : negative ^[47]	NA	<i>Tha.</i> : + ^[47] <i>Cortex</i> : negative ^[47]	<i>OB</i> : negative ^[47]	NA

Legend: Nc./Ncc. = nucleus/nuclei; DMNV = Dorsal motor nucleus of the vagus nerve; Nc. Sol. Trac. = Nucleus of the solitary tract; Nc. Trigem. = Nucleus of the spinal tract of V; Nc. Hyp. = Nucleus hypoglossus; Nc. Coch. = Nc. cochlearis; Vest. Compl. = Vestibular nuclear complex; Nc. Cun = Nucleus cuneatus; Olive = olivary nuclei; Ret. Form.: reticular formation; Centr. Grey = Central Grey matter; Rostr. Coll. = Rostral Colliculus; Med. Gen. Nc. = Medial geniculate nucleus; Tha. = Thalamus; Hyp. = Hypothalamus; Hip. = Hippocampus; BG = Basal ganglia; CS = Corpus striatum; Caud. = Nc. caudatus; Put = Putamen; Sept. = Septal nuclei; Claustr. = Claustrum; OB = Olfactory bulb; LoP = Lobus piriformis; (+) = weak, + = mild, ++ = moderate, +++ = severe lesions; NA = not available; *Frontal Cortex^[11,16,18,19,24,25,28,29,30,31,43], or cerebral Cortex^[7,27,40,47]; references are to the main text.

Table S2: PrP^{Sc} profiles in brainstem described in literature for C-, H- and L-type BSE infected cattle (literature review)

BSE	Brainstem						Others/Remarks
	DMNV	Nc. Sol. Trac.	Nc. Trigem.	Olive	Ret. Form	Brainstem in general	
C-type (field)	PrP ^{Sc} : +++ ^[45] PART ^[40,42] , F-C-PART+++ ^[44] , C-PART-CoL ^[45] , CoL+ ^[44] ITMG ^[42,45] + ^[44] , STEL++ ^[44] ITNR ^[40] + ^[44] , less ITNR ^[45] PNER ^[40] + ^[44] , LIN+ ^[44]	PrP ^{Sc} : +++ ^[45] PART ^[40,42,19] , Agg. ^[19] , F-C-PART+++ ^[44] , C-PART-CoL ^[45] , CoL+ ^[44] , ITMG ^[45,19] + ^[44] , STEL++ ^[44] ITNR ^[45,19] + ^[44] , PNER+ ^[44] LIN+ ^[44]	PrP ^{Sc} : +++ ^[45] PART ^[40,42,19] , C-PART-CoL ^[45] , ITMG ^[19,45] , ITNR ^[19,45] , Agg. ^[19]	PrP ^{Sc} : +++ ^[45] PART+++ ^[44] , F-C-PART+ ^[44] , C-PART-CoL ^[45] ITMG ^[45] + ^[44] , ITNR ^[40,45] ++ ^[44] LIN+ ^[44]	PrP ^{Sc} : +++ ^[45] PART ^[42] ++ ^[44] , C-PART-CoL ^[45] , C-PART+ ^[44] CoL ^[42] + ^[44] , ITMG ^[45] , STEL+ ^[44] , ITNR ^[40,42,15] , PNER+ ^[44] , LIN ^[42] +++ ^[44]	PrP ^{Sc} : +++ ^[7] PART ^[7] , F-C-PART +++ ^[41] F-C-PART-CoL ^[43] , CoL++ ^[41] , STEL ^[7,41] , ITNR ^[7,43] ++ ^[41] , LIN ^[7,43] PNER ^[41]	Brainstem mostly affected ^[43] <i>Vest. Compl.:</i> ITNR ^[19,40] , ITMG ^[19] , STEL ^[19] , PART ^[19] , LIN ^[19] Nc. Hyp: STELL ^[42] , ITNR ^[19,40] , PART ^[19]
C-type (IC)	PrP ^{Sc} : + ^[28]	PrP ^{Sc} : +++ ^[28]	PrP ^{Sc} : +++ ^[28]	NA	NA	PrP ^{Sc} : +++ ^[28] PART, STEL, ITNR ^[24]	NA
H-type (field)	PrP ^{Sc} : + ^[23]	PrP ^{Sc} : ++(+) ^[22] or + ^[23] F-PART ^[22] , PNER ^[22] , LIN ^[22]	PrP ^{Sc} : +++ ^[22] or + ^[23] F-PART ^[22] , PNER ^[22] , LIN ^[22]	PrP ^{Sc} : + ^[23] ITNR ^[22]	ITNR ^[22]	F-C-PART ^[22,23] , Agg. ^[8] , ITNR/ITMG ^[8,23] , selected Ncc.: ITNR ^[22] , PNER+ ^[22] LIN(+) ^[22]	<i>Nc. Cun.:</i> ITNR ^[22] + ^[23] <i>Nc. Hyp:</i> PrP ^{Sc} + ^[23]
H-type (IC)	No ITNR ^[27] ITMG ^[61]	ITMG ^[61]	ITMG ^[61]	NA	NA	PrP ^{Sc} : +++ ^[27,30,26] F-C-PART ^[31,26] , CoL ^[27] , ITMG ^[8,10,61] , ITNR ^[26,27] , PNER ^[26] , LIN ^[26]	Distinct ITMG/STEL ^[31] or ITMG ^[61] WM: ITMG ^[26] No ITNR with SAF32 and B103 (N-terminal) ^[26]

L-type (field)	<i>PrP^{Sc}</i> : (+) ^[8] Negative ^[7] Agg. ^[42]	Agg. ^[42]	<i>PrP^{Sc}</i> : (+) ^[8] Agg. ^[42]	NA	Agg. ^[42]	<i>PrP^{Sc}</i> : (+) ^[7] No PL ^[46]	ITNR/ExNTR ^[8] Similar to C- Type ^[46] , consistent ^[30] with [46] (L-type IC)
L-type (IC)	ITNR ^[61]	ITNR ^[61]	ITNR ^[61]	NA	NA	<i>PrP^{Sc}</i> : +++ ^[29,30] F-C-PART ^[29,30] , CoL ^[30] ITNR ^[14,61] , PNER ^[12]	Similar to C-Type ^[25] PNER prominent ^[31]
L-type (oral)	<i>PrP^{Sc}</i> : ++ ^[47]	NA	NA	NA	NA	<i>PrP^{Sc}</i> : +++ ^[47] F-C-PART ^[47] , <i>Nc. Cun</i> : PNER ^[47]	No PL ^[47]

Legend: DMNV = Dorsal motor nucleus of the vagus nerve; Nc. Sol. Trac. = Nucleus of the solitary tract; Nc. Trigem. = Nucleus of the spinal tract of V; Nc. Hyp. = Nucleus hypoglossus; Vest. Compl. = Vestibular nuclear complex; Nc. Cun = Nucleus cuneatus; Olive = olivary nuclei; Ret. Form.: reticular formation; Nc./Ncc. = nucleus/nuclei; PrP^{Sc} = quantity of PrP^{Sc}; (+) = weak, + = mild, ++ = moderate, +++ = severe accumulation of PrP^{Sc}; PART = PrP^{Sc} deposition on cell surface in different appearance: F-G-PART-CoL = fine (F) and/or coarse (C) PART accumulation up to a coalescing (CoL) pattern; ITMG = intramicroglial; STEL = stellate; ITNR = intraneuronal; PNER = perineuronal; LIN = linear; Agg. = aggregates; PL = plaques; NA = not available; anti-PrP antibodies used recognize the core region of the protein: F99^[7,8,22,23,24,26,27,29,42,47]; R145^[19,30,31,46]; 6H4^[25,41,43]; T1^[28,45]; 12F10^[8]; C15S^[44]; L42^[43]; SAF84^[40]; F99/6C2^[61]; references are to the main text.

Table S3: PrP^{Sc} profiles in different brain regions described in literature for C-, H- and L-type BSE infected cattle (literature review)

BSE	Cerebellum	Midbrain	Thalamus	Hypothalamus and Hippocampus	Cerebrum	Other brain regions	Remarks
C-type (field)	<i>Cortex:</i> F-C-PART ^[41] ; ITNR ⁽⁺⁾ ^[41] ; PNER ^[41,43] ; STEL ⁺⁺ ^[41,43] <i>MLay:</i> STEL ⁺⁺ ^[45] <i>Medulla:</i> PrP ^{Sc} ⁺⁺ ^[45] , F-C-PART ^[43,45] ; ITNR ^[43,45] ; STEL ^[43] ; LIN ^[43,45] <i>Vermis:</i> STEL ^[43] ; F-C-PART ^[43]	<i>PrP^{Sc}:</i> ⁺⁺⁺ ^[25,45] PART ^[25] , F-C-PART-CoL ^[43,45] , PART-CoL ⁺⁺ ^[41] , STEL ^[43] ⁺⁺ ^[41] , ITNR ^[41,43,45] (Red Nc. ⁴⁰) PNER ^[41,43] , LIN ^[41,43] , PL ^[25] <i>Subst. nigra:</i> PART ^[40] <i>Centr. Grey:</i> PL ^[40] (not in ^[19]), ITNR ^[19] , STEL ^[19] , PART ^[19] , Agg ^[19]	<i>PrP^{Sc}:</i> ⁺⁺⁺ ^[7,45] PART ^[7,19,40,43] , F-C-PART-CoL ^[43,45] , PART-CoL ⁺⁺ ^[41] , STEL ^[7,19,43,45] , ⁺ ^[41] , ITNR ^[7,19,40,43,45] ⁺⁺ ^[41] , PNER ^[45] ⁺⁺ ^[41] , LIN ^[7,19,43,45] ⁺⁺ ^[41] , PL ^[40] , Agg. ^[19]	<i>Hyp:</i> PrP ^{Sc} ⁺⁺⁺ ^[45] ITNR ^[19,40,45] , F-C-PART-CoL ^[45] , Agg. ^[19] , STEL ^[19,45] PNER ^[19,45] ⁺⁺ ^[41] , LIN ^[19,45] <i>Hip:</i> PrP ^{Sc} ⁺⁺ ^[45] F-C-PART in GLay ^[45] , STEL ^[41,43] in Str. Oriens / MLay ^[45] , ITNR ^[41] in Str. Pyr. ^[45] , PNER ^[41,43] , LIN in Str. Oriens / MLay ^[45]	<i>Cortex:</i> PrP ^{Sc} ⁺ ^[7,45] PART ^[2] , ⁽⁺⁾ ^[19,41] , F-PART ^[45] STEL ^[7,19,45] ⁺⁺ ^[41] , ITNR ^[7,45] ⁽⁺⁾ ^[19] PNER ^[40] , LIN ^[7,19,41,45] , PL ^[40]	<i>CS:</i> F-C-PART ^[45] ⁺ ^[41] , CoL ^[41] , STEL ^[41,45] , ITNR ^[45] , LIN ^[41,45] <i>OB^[7], LoP^[7]:</i> PrP ^{Sc} ⁺ PART, STEL, ITNR, LIN <i>Caud-Put:</i> ITNR ^[19] , STEL ^[19] , PNER ^[19,40] , LIN ^[19] , Agg ^[19] <i>Sept.:</i> ITNR ^[19] , STEL ^[19] , PART ^[19] , LIN ^[19] , ⁽⁺⁾ PNER ^[19] , ⁽⁺⁾ Agg ^[19] <i>Claustr.:</i> STEL ^[19]	Cerebral Cortex the least affected ^[43]
C-type (IC)	WM: PrP ^{Sc} ⁺⁺⁺ ^[28] GLay: ⁺ ⁽⁺⁾ ^[28] <i>In general:</i> PART ^[24] , STEL ^[24] , ITNR ^[24]	NA	<i>PrP^{Sc}:</i> ⁺⁺⁺ ^[28] PART ^[24] , STEL ^[24] , ITNR ^[24]	NA	<i>Cortex:</i> PrP ^{Sc} ⁺ ⁽⁺⁾ ^[28] PART ^[24] , STEL ^[24] , ITNR ^[24]	<i>OB^[24], BG^[24]:</i> PART, STEL	NA
H-type (field)	<i>PrP^{Sc}:</i> negative ^[23]	<i>PrP^{Sc}:</i> ⁺ ^[23] PART, ITNR, ITMG ^[23]	<i>PrP^{Sc}:</i> ⁺ ^[23] PART, ITNR, ITMG ^[23]	<i>Hip:</i> PrP ^{Sc} negative ^[23]	<i>Cortex:</i> PrP ^{Sc} negative ^[23]	<i>BG:</i> PrP ^{Sc} negative ^[23]	NA
H-type (IC)	<i>Cortex:</i> STEL ^[26] <i>M/Lay:</i> PrP ^{Sc} ⁽⁺⁾ ^[27] or ⁺ ^[30] , PART ^[27] , multifocal ^[30]	<i>PrP^{Sc}:</i> PrP ^{Sc} ⁺⁺⁺ ^[27] F-C-PART ^[26] , ITMG ^[27] in WM ^[26] , ITNR ^[27] in different Ncc.	F-C-PART ^[26] , STEL ^[26] ITNR ^[26] , LIN ^[26] , PNER ^[26]	<i>Hyp:</i> PrP ^{Sc} ⁺⁺⁺ ^[26] F-C-PART ^[26] , STEL ^[26] <i>Hip:</i> PrP ^{Sc} ⁺⁺ ^[27] CoL ^[27] , STEL ^[26] ,	<i>Cortex:</i> PrP ^{Sc} ⁺⁺⁺ ^[26] PART ^[30] , F-C-PART ^[26,27] , CoL ^[27] , STEL ^[26,27,30] , ITMG ^[27] , ITNR ^[25]	<i>BG^[26]:</i> PrP ^{Sc} ⁺⁺⁺ F-C-PART, STEL, ITNR, PNER, LIN <i>CS:</i> ⁺ PL ^[26]	Extensive PART, but distinct ITMG/STEL ^[31] No ITNR with SAF32 and B103 (N-terminal) ^[26]

	WM: negative ^[27] , STEL ^[30] , ITMG ^[26] , PL ^[26] Ncc.: PrP ^{Sc} positive ^[27] <i>In general</i> : F-C- PART ^[26]			WM: ITMG ^[26] , PL ⁺ ^[26]	rarely ^[27] , PNER ^[26,27] , LIN ^[26] , PL ^[26] WM: (+) C- PART ^[27] , ITMG ^[26] , PL ^[26] rarely ^[30]		
L-type (field)	<i>MLay</i> : PrP ^{Sc} ⁺ ^[7] PL ^[7]	NA	PL ^[7]	NA	<i>Cortex</i> /WM: PL ^[7]	<i>OB</i> : PL ^[7]	No PL ^[46] , pattern similar to C-type ^[46] , consistent ^[30] with ^[46] (L-type IC)
L-type (IC)	<i>M/GLay</i> : PrP ^{Sc} +++ ^[30] , homogenous ^[30] Ncc.: F-C-PART ^[29] <i>In general</i> : PNER ^[24]	<i>Centr. Grey</i> : F-C-PART ^[29] , PL (+) ^[29]	<i>PrP^{Sc}</i> : +++ ^[25] PART ^[25] , F-C- PART+++ ^[29] ITNR++ ^[29] , PNER ^[24] , PL ^[25] ; (+) ^[29]	PNER ^[24]	<i>Cortex</i> : F-C- PART ^[29] , ITNR ⁺ ^[29] , PL in deep grey layers ^[24,29] WM: C-PART ^[30] , PNER ^[30,24] , PL ^[24,27,30] (+) ^[29]	<i>BG</i> : PL(+) ^[29]	Like C-type topography ^[25] In midbrain and thalamus mostly periaquae-ductual areas affected ^[25] Extensive PART, distinct PNER ^[31]
L-type (oral)	NA	NA	<i>PrP^{Sc}</i> : +++ ^[47] F-C-PART ^[47] , PNER ^[47]	NA	NA	NA	No PL detectable ^[47]

Legend: Nc./Ncc. = nucleus/nuclei; MLay = Molecular layer; GLay = Granular layer; WM = white matter; Subst. = Substantia; Centr. Grey = Central grey matter; Hyp. = Hypothalamus; Hip. = Hippocampus; Str. = Stratum; Pyr. = Stratum pyramidale; BG = Basal ganglia; CS = Corpus striatum; Caud.-Put. = Nc. caudatus-Putamen; Sept. = Septal nuclei; OB = Olfactory bulb; LoP = Lobus piriformis; Claustr.: Claustrum; PrP^{Sc} = quantity of PrP^{Sc}; (+) = weak, + = mild, ++ = moderate, +++ = severe accumulation of PrP^{Sc}; PART = PrP^{Sc} deposition on cell surface in different appearance: F-G-PART-CoL = fine (F) and/or coarse (C) PART accumulation up to a coalescing (CoL) pattern; ITMG = intramicroglial; STEL = stellate; ITNR = intraneuronal; PNER = perineuronal; LIN = linear; Agg. = aggregates; PL = plaques; NA = not available; anti-PrP antibodies used recognize the core region of the protein: F99^[7,8,22,23,24,26,27,29,42,47]; R145^[19,30,31,46]; 6H4^[25,41,43]; T1^[28,45]; 12F10^[8]; C15S^[44]; L42^[43]; SAF84^[40]; references are to the main text.