

**Supplementary table 1: Larger SN echogenic areas and SN echogenic status in the general community by sex and age**

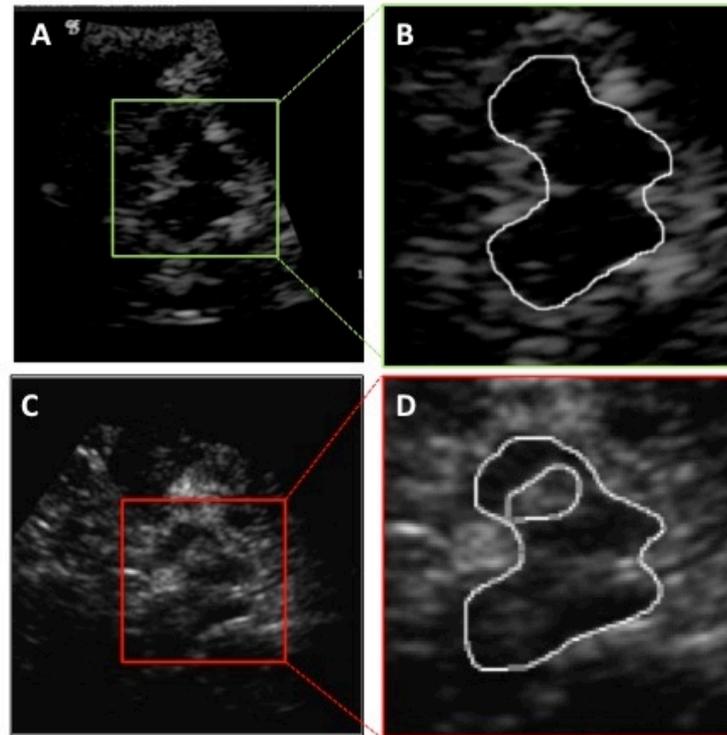
Sex / age groups	Entire population (n=473)		Non-parkinsonian population (n=447)	
	Median (25 <sup>th</sup> – 75 <sup>th</sup> %) of SN <sub>L</sub> [cm <sup>2</sup> ]	Prevalence [95%CI] of SN hyperechogenicity	Median (25 <sup>th</sup> – 75 <sup>th</sup> %) of SN <sub>L</sub> [cm <sup>2</sup> ]	Prevalence [95%CI] of SN hyperechogenicity
<b>Women (n=226)</b>	0.13 (0.09–0.16)	22.6% [17.6–28.5]	0.12 (0.09–0.16)	21.4% [16.4–27.4]
<b>55-64 (n=94)</b>	0.13 (0.10–0.16)	21.3% [14.1–30.7]	0.13 (0.10–0.16)	20.4% [13.4–29.8]
<b>65-74 (n=67)</b>	0.12 (0.08–0.16)	22.4% [14.0–33.8]	0.12 (0.08–0.16)	21.5% [13.2–33.1]
<b>75-94 (n=65)</b>	0.12 (0.09–0.18)	24.6% [15.7–36.4]	0.12 (0.08–0.17)	22.8% [13.7–35.3]
<b>Men (n=247)</b>	0.15 (0.11–0.18)	28.7% [23.5–34.7]	0.14 (0.11–0.17)	24.6% [20.2–29.5]
<b>55-64 (n=100)</b>	0.14 (0.10–0.17)	21.0% [14.1–30.1]	0.14 (0.10–0.17)	20.2% [13.4–29.2]
<b>65-74 (n=81)</b>	0.15 (0.12–0.19)	35.8% [26.2–46.7]	0.15 (0.11–0.18)	31.6% [22.2–42.7]
<b>75-94 (n=66)</b>	0.15 (0.12–0.18)	31.8% [21.8–43.8]	0.14 (0.11–0.17)	22.8% [13.7–35.3]
<b>Overall (n=473)</b>	0.14 (0.10–0.18)	25.8% [22.1–30.0]	0.13 (0.10–0.17)	23.0% [19.9–26.5]
<b>55-64 (n=194)</b>	0.13 (0.10–0.17)	21.1% [16.0–27.4]	0.13 (0.10–0.17)	20.3% [15.2–26.6]
<b>65-74 (n=148)</b>	0.14 (0.10–0.18)	29.7% [22.9–37.6]	0.13 (0.10–0.18)	27.0% [20.3–34.8]
<b>75-94 (n=131)</b>	0.14 (0.10–0.18)	28.2% [21.2–36.5]	0.14 (0.10–0.17)	22.8% [16.0–31.4]

Numbers of participants in the first column are given for the entire population. P-values for sex differences were <0.001 for continuous variable SN<sub>L</sub> (larger area of substantia nigra echogenicity of the two sides) in both the entire population and the non-parkinsonian population. However, sex did not significantly influence the prevalence of SN hyperechogenicity (p=0.1). Age did influence neither on SN<sub>L</sub> as a continuous variable nor on SN echogenic status.

**Supplementary table 2: Diagnostic accuracy of SN hyperechogenicity for the differentiation of PD versus non-PS subjects by age groups**

Age groups	FP (n)	FN (n)	TN (n)	TP (n)	Sensitivity (%) [95%CI]	Specificity (%) [95%CI]	PPV (%) [95%CI]	NPV (%) [95%CI]
55-64 years (n=193)	39	0	153	1	100.0 [16.8–100.0]	79.7 [73.4–84.8]	2.5 [0.0–14.0]	100.0 [97.1–100.0]
65-74 years (n=145)	38	0	103	4	100.0 [45.4–100.0]	73.1 [65.2–79.7]	9.5 [3.2–22.6]	100.0 [95.7–100.0]
75-94 years (n=126)	26	2	88	10	83.3 [54.0–96.5]	77.2 [68.6–84.0]	27.8 [15.7–44.1]	97.8 [91.8–99.9]
p-values for age trends					ns	ns	<0.01	ns
Total* (n=464)	103	2	344	15	88.2 [64.4–98.0]	77.0 [72.8–80.6]	12.7 [7.8–20.0]	99.4 [97.8–100.0]

Substantia nigra hyperechogenicity (SN+), defined as  $\geq 0.18 \text{ cm}^2$  for the larger area of echogenicity of the two sides (SN<sub>L</sub>). FP, false positive; FN, false negative; TN, true negative; TP, true positive; PPV, positive predictive value; NPV, negative predictive value; ns, non-significant. \* The 9 subjects with a parkinsonian syndrome not fulfilling PD criteria (PS subjects) were excluded from this analysis.



**Supplementary figure 1.** Transcranial sonography images of mesencephalic scanning planes showing typically butterfly-shaped mesencephalic brainstems from a non-parkinsonian subject with a normal midbrain echogenicity (A and B) and a PD subject with an enlarged midbrain echogenicity at the area of the substantia nigra (SN hyperechogenicity, C and D).