

## Aberystwyth University

### *Haplotype structure, adaptive history and associations with exploratory behaviour of the DRD4 gene region in four great tit (*Parus major*) populations*

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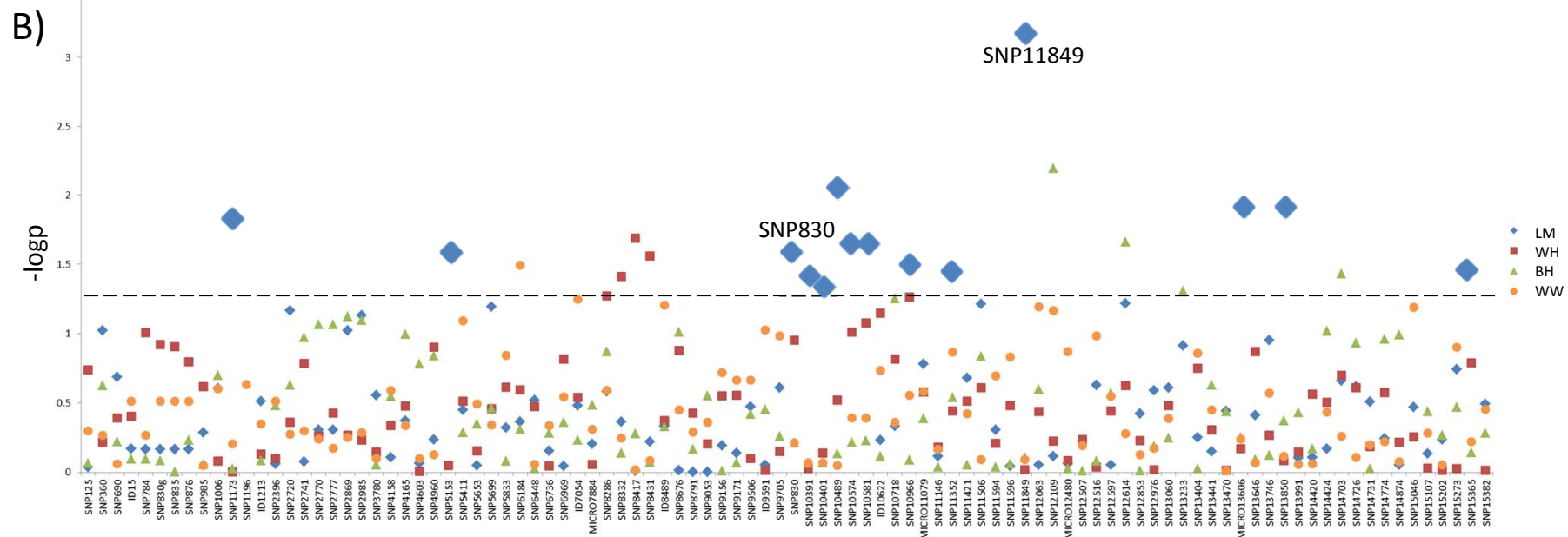
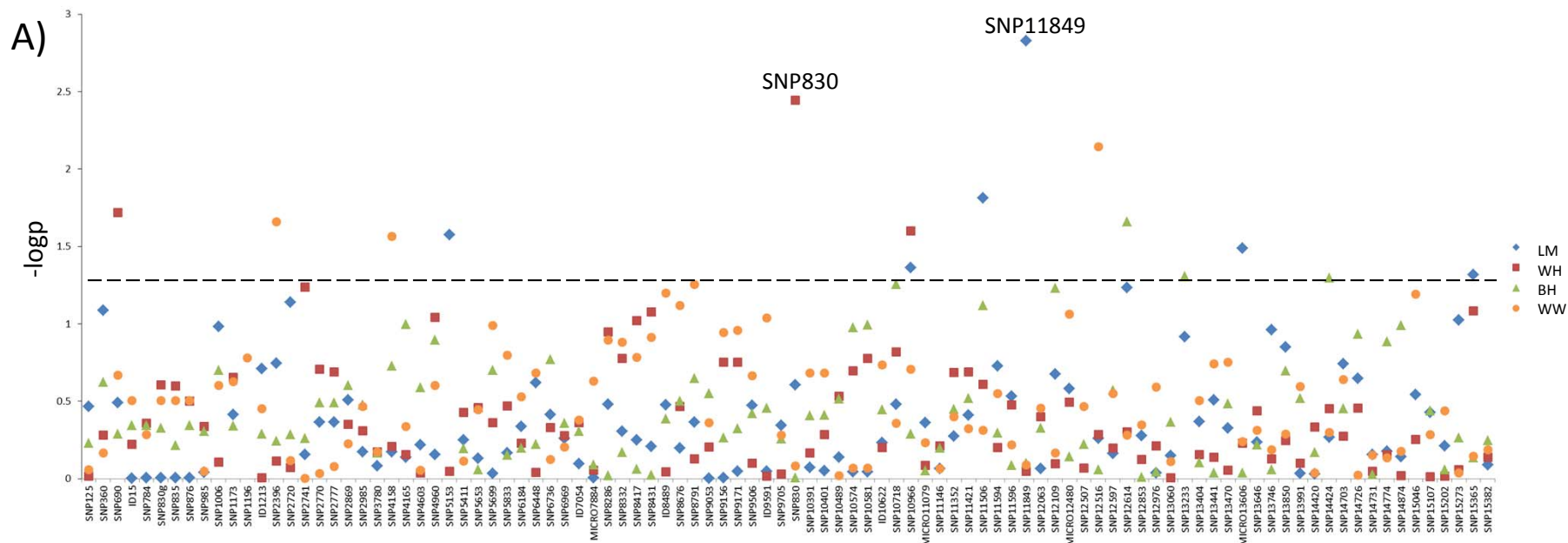
## Supplementary file 1

In addition to the tests for association between *DRD4* polymorphisms and exploratory behaviour while accounting for or excluding first-degree relatives as described in the main article, we also tested the associations while accounting for the complete known relatedness structure (including lower-degree relatedness). This was done in order to show the robustness of the results. We calculated kinship coefficients between all individuals from pedigrees using the R package QTLRel (Cheng et al. 2011). Kinship groups were defined from breeding records of banded birds of the years 1993 to 2007 (LM), 1991 to 2007 (WH), 1991 to 2007 (BH) and 1985 to 2007 (WW). After pooling the minor alleles of the four microsatellites, additive and overdominant allele effects were tested for each locus using a mixed-model analysis, which incorporates the kinship matrix, as implemented in QTLRel (Cheng et al. 2010). For Westerheide we also included study year as fixed effect. The study-wide significance of the multiple single-marker tests in each population sample was evaluated by permuting the genotypes 200 times.

The plot of association results (p-values) (Supplementary Figure 1) across all loci showed very similar patterns in comparison to the association results presented in the main text (Figure 2). The strongest association signals for the additive allele effect model were observed at the originally reported SNP830 in the Westerheide population and SNP11849 in the Lauwersmeer population (Supplementary Figure 1A). The sets of nominal significant signals in each population, however, were not study-wide significant on the 5% level. The strongest association signals for the overdominant allele effect model were found at SNP11849 with a clustering of significant association signals between SNP830 and SNP11849 in the Lauwersmeer population (Supplementary Figure 1B). Analog to the results in the main document, only the set of nominal significant overdominant association signals in the Lauwersmeer was study-wide significant with a permutation p-value of less than 0.5%. This underlines the robustness of the results and indicates that non-first-degree relatedness structures have only an unimportant influence on the association outcomes in our study.

## References

- Cheng R, Lim JE, Samocha KE, Sokoloff G, Abney M, Skol AD, Palmer AA. 2010. Genome-wide association studies and the problem of relatedness among advanced intercross lines and other highly recombinant populations. *Genetics* 185:1033-1044.
- Cheng R, Abney M, Palmer AA, Skol AD. 2011. QTLRel: an R package for genome-wide association studies in which relatedness is a concern. *BMC Genetics* 12: 66.



**Supplementary Figure 1.** Single-marker associations (p-values) in each population while accounting for the detailed relatedness structure. A) Additive allele effect model; additive effect of most frequent allele for the four microsatellites. B) Overdominant allele effect model; enlarged symbols highlight the study-wide significant set of associations in Lauwersmeer. Dashed line indicates nominal 5% significance threshold.

Supplementary table 1: Primer information for each indel (ID) and microsatellite (MICRO).

Locus	Forward primer	Reverse primer
ID15	CCTCTGGAAGCAGAATTTGAGGA	GCCCCAAAGTTCCTTACTCTT
ID1213	TCACATCTGGGCTGAGGTTT	GCAGGATGCACTTCAAAGG
ID7054	CCAGCAAAGCCTCTTATCCA	GCAGCCACTCCAAACTGAAT
MICRO7884	CTATGAGCACTGGCTGGCTA	GCCCCTTGTCATGTCTCACT
ID8489	GGGTTTGTACCTGGGTGAGA	ACCTGGAAATGTTGGCTCTG
ID9591	GGAGGGTGTCTGCCCTAAT	GAGTCAGTCCTGGTGTGGTG
ID10622	GCTGCCTTTTCCCTGAGTGCTT	TGTCCAGCAGAAGAGGAAAGCA
MICRO11079	CTGGTCTGCTGTCTTTGTTGG	GGACATCTGGGAAATGAGCTT
MICRO12480	TCTCAGCTTTCTTGCCTCACG	ACAGCACRCAGCTCTTCCAG
MICRO13606	GCAGGACAAGTGACCCTC	AATCAAGCCCAAGGTGAGCA

Supplementary table 2: Allele names and minor allele frequency (MAF) of each single nucleotide polymorphism (SNP), indel (ID) and microsatellite (MICRO) in each population. For microsatellites all minor allele frequencies are listed.

Locus	Major/minor allele(s)	MAF_LM	MAF_WH	MAF_BH	MAF_WW
SNP125	G/A	0.2139	0.2384	0.2821	0.1937
SNP360	G/C	0.1198	0.0615	0.0631	0.1000
SNP690	A/G	0.3823	0.3636	0.3932	0.3842
ID15	+/-	0.0994	0.1076	0.1165	0.0576
SNP784	G/A	0.0948	0.1153	0.1127	0.0542
SNP830g	G/T	0.0968	0.1111	0.1185	0.0472
SNP835	T/G	0.0953	0.1076	0.1170	0.0581
SNP876	T/G	0.0969	0.1076	0.1195	0.0581
SNP985	G/A	0.0603	0.0775	0.0271	0.0162
SNP1006	G/A	0.0644	0.0692	0.0631	0.0736
SNP1173	G/C	0.4345	0.4841	0.5150	0.4285
SNP1196	T/C	0 0	0 0.0354		
ID1213	+/-	0.1658	0.1171	0.1116	0.1692
SNP2396	G/A	0.4371	0.4596	0.4166	0.5000
SNP2720	C/T	0.1082	0.0483	0.0421	0.0891
SNP2741	T/C	0.1693	0.1140	0.1935	0.1735
SNP2770	T/C	0.1868	0.1428	0.1950	0.1984
SNP2777	G/A	0.1862	0.1328	0.1960	0.1976
SNP2869	T/G	0.4974	0.5620	0.4656	0.4692
SNP2985	C/A	0.4318	0.4385	0.5820	0.5420
SNP3780	C/T	0.0595	0.0307	0.0337	0.0703
SNP4158	C/T	0.2357	0.2692	0.2743	0.1718
SNP4165	G/T	0.1717	0.0873	0.0965	0.1653
SNP4603	C/T	0.1848	0.1250	0.1274	0.2070
SNP4960	A/C	0.2696	0.3492	0.3750	0.2539
SNP5153	A/T	0.0051	0 0	0	
SNP5411	C/T	0.1282	0.1349	0.1111	0.1614
SNP5653	G/A	0.3163	0.1769	0.1893	0.2653

SNP5699	A/C	0.4869	0.3888	0.4329	0.5550		
SNP5833	C/T	0.2434	0.3095	0.3939	0.2248		
SNP6184	G/A	0.2307	0.2968	0.3484	0.2038		
SNP6448	G/A	0.5280	0.4609	0.4400	0.4884		
SNP6736	A/G	0.2474	0.2076	0.2330	0.2807		
SNP6969	C/A	0.3698	0.3000	0.4257	0.2558		
ID7054	-/+	0.2576	0.2578	0.4029	0.1807		
MICRO7884	309/307/311/313	0.2600/0.0770/0.0688	0.2500/0.0312/0.0550	0.4030/0.0340/0.0097			
		0.2270/0.0780/0.0468					
SNP8286	A/G	0.3219	0.4206	0.4504	0.2738		
SNP8332	C/T	0.3567	0.4843	0.5350	0.3267		
SNP8417	A/G	0.3377	0.4354	0.4948	0.3223		
SNP8431	A/G	0.3659	0.4846	0.5190	0.3565		
ID8489	+/-	0.0892	0.1111	0.1067	0.0769		
SNP8676	G/A	0.4097	0.2419	0.2552	0.3720		
SNP8791	G/A	0.3520	0.4307	0.4642	0.3038		
SNP9053	G/A	0.0076	0.0076	0.0048	0.0153		
SNP9156	A/C	0.3592	0.5820	0.4675	0.3873		
SNP9171	C/T	0.3814	0.5710	0.4756	0.4087		
SNP9506	C/T	0.0309	0.0538	0.0392	0.0232		
ID9591	-/+	0.0765	0.0468	0.0533	0.0576		
SNP9705	G/A	0.1102	0.0769	0.0505	0.0793		
SNP830	C/T	0.3429	0.3359	0.3030	0.3425		
SNP10391	T/C	0.2193	0.2538	0.2128	0.2364		
SNP10401	C/G	0.2230	0.2500	0.2184	0.2325		
SNP10489	A/G	0.2938	0.3000	0.2626	0.2952		
SNP10574	G/C	0.3560	0.4285	0.3588	0.3730		
SNP10581	C/T	0.3608	0.4307	0.3518	0.3818		
ID10622	+/-	0.0714	0.1328	0.0825	0.0346		
SNP10718	C/T	0.1288	0.0230	0.0200	0.0275		
SNP10966	G/A	0.1256	0.1209	0.1702	0.1708		
MICRO11079	312/304/306/309	0.4000/0.0210/0.0076	0.2340/0.0078/0.0390	0.3520/0.0150/0.0051			
		0.3140/0/0.0232					
SNP11146	G/A	0.0031	0.0153	0.0057	0.0041		
SNP11352	T/G	0.3945	0.2241	0.2611	0.2897		
SNP11421	T/C	0.3917	0.2096	0.2252	0.2929		
SNP11506	C/T	0.1542	0.1015	0.3269	0.1920		
SNP11594	A/C	0.4102	0.2343	0.2446	0.2913		
SNP11596	A/G	0.2422	0.0887	0.0500	0.0859		
SNP11849	C/T	0.0838	0.1020	0.0949	0.0990		
SNP12063	T/G	0.1929	0.0887	0.0500	0.1000		
SNP12109	G/A	0.5930	0.4250	0.3437	0.4471		
MICRO12480	393/391/389/387/397/395/392/383/385	0.074/0.044/0.026/0.010/0.008/0.059/0/0.003	0.079/0.032/0.032/0.032/0/0/0/0	0.092/0.020/0.031/0.026/0/0/0/0	0.035/0.058/0.035/0.012/0.008/0/0.004/0		
SNP12507	C/A	0	0.0096	0.0066	0.0043		
SNP12516	T/G	0.5170	0.4083	0.2890	0.3418		
SNP12597	C/T	0.0031	0.0288	0.0281	0.0153		
SNP12614	C/T	0.0204	0.0245	0.0281	0.0083		
SNP12853	C/T	0.2732	0.1428	0.0934	0.1176		
SNP12976	A/C	0.5030	0.3809	0.2906	0.3445		
SNP13060	C/G	0.1974	0.2153	0.2553	0.2362		
SNP13233	T/C	0.0051	0	0.0153	0		
SNP13404	G/A	0.3388	0.3750	0.3888	0.4000		
SNP13441	G/A	0.2934	0.2592	0.2797	0.2207		

SNP13470	C/T	0.5130	0.4218	0.4888	0.4370
MICRO13606	327/339/329	0.0794/0	0.0859/0	0.1600/0.0360	0.1085/0
SNP13646	C/T	0.1564	0.1538	0.1761	0.1535
SNP13746	A/G	0.3608	0.2421	0.2043	0.2165
SNP13850	C/A	0.1056	0.1190	0.1290	0.1181
SNP13991	G/A	0.2577	0.2983	0.1988	0.3031
SNP14420	C/T	0.0589	0.0781	0.0430	0.0669
SNP14424	C/T	0.2368	0.2661	0.1808	0.2559
SNP14703	G/A	0.0534	0.0538	0.2261	0.0934
SNP14726	G/T	0.1410	0.2338	0.3315	0.1835
SNP14731	G/A	0.1914	0.1666	0.0618	0.1434
SNP14774	C/T	0.2293	0.2500	0.3333	0.2519
SNP14874	G/A	0.1603	0.1290	0.0736	0.1302
SNP15046	A/T	0.0335	0 0	0.0118	
SNP15107	C/G	0.1871	0.0396	0.0578	0.0859
SNP15202	G/A	0.0641	0.0737	0.0600	0.1031
SNP15273	A/G	0.2557	0.2870	0.4034	0.2882
SNP15365	C/T	0.0625	0.0967	0.2701	0.1150
SNP15382	C/T	0.1822	0.1507	0.0858	0.1875

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