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ORIGINAL PAPER

Most significant genome regions involved in the control of earliness traits in bread wheat, as revealed by QTL meta-analysis

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Abstract Earliness is one of the most important adaptation traits in plant breeding. Our purpose was to identify the genome regions of bread wheat involved in the control of earliness and its three components: photoperiod sensitivity (PS), vernalization requirement (VR) and intrinsic earliness (IE). A QTL meta-analysis was carried out to examine the replicability of QTL across 13 independent studies and to propose meta-QTL (MQTL). Initial QTL were projected on a recent consensus map (2004). Quality criteria were proposed to assess the reliability of this projection. These criteria were based on the distances between markers in the QTL regions. Chromosomes of groups 2 and 5 had a greater incidence on earliness control as they carry the known, major genes *Ppd* and *Vrn*. Other chromosome regions played an intermediate role in earliness control: 4A [heading date (HD) Meta-QTL], 4B (HD MQTL), 2B (VR MQTL) and 5B (IE MQTL). Markers at this four MQTL should prove helpful in marker-assisted selection, to better control earliness.

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Introduction

Earliness can be considered as an adaptation trait (Worland 1996). Its control has been one of the main explanations for the gradual extension of wheat cultivation (Stelmakh 1990; Law and Worland 1997). Nowadays, earliness remains a major factor of variation for agronomic traits, and one of the critical traits which must be considered when breeding a variety. For this reason, the modern methodologies used to investigate the genome, such as QTL and gene mapping, are useful tools for breeders. One of the main issues regarding these methodologies is to determine reliable markers that can be implemented in the context of marker-assisted selection (MAS) programs.

Thanks to the simultaneous development of molecular biology and the theory underlying QTL detection, as well as the corresponding softwares, an increasing number of markers, genetic maps and QTL are now readily available. This is particularly the case of earliness at flowering that is frequently measured, not only for its direct interest but also in many cases as a factor of variation when investigating other agronomic traits. In order to better control and understand this complex trait, earliness can be broken down into its three components: photoperiod sensitivity (PS), vernalization requirement (VR) and intrinsic earliness (IE). QTL for earliness and its components are thus widely available, but little is known of the genetic control of earliness in wheat when compared with other species where genes and biochemical pathways are well documented, such as legumes (Weller et al. 1997) or Arabidopsis (Putterill et al. 2004).

In wheat, earliness QTL and genes mapping initially focused on specific chromosomes because chromosome

recombinant lines were employed. This material was targeted during cytogenetic studies in the 1970s which mainly concerned group 5 chromosomes and VR (e.g., Galiba et al. 1995; Kato et al. 1998; Leonova et al. 2003; Toth et al. 2003) or IE (Kato et al. 1999), and group 2 chromosomes and PS (Worland 1996). More recently, the emergence of microsatellite markers has enabled the construction of relatively dense genetic maps, and different authors have developed approaches at the whole genome level (Börner et al. 2002; Shindo et al. 2002, 2003; Gervais et al. 2003; Hanocq et al. 2003, 2004; Kulwal et al. 2003; Sourdille et al. 2000, 2003). Consensus QTL maps could be of considerable value to wheat breeders, but at present none is available.

A method called meta-analysis was first proposed to integrate and summarize results from separate studies (Glass 1976; Khatkar et al. 2004). Meta-analysis was then adapted to genetic and QTL studies (Goffinet and Gerber 2000). Finally, this method has been used successfully in both animal and plant breeding studies (Belknap and Atkins 2001; Khatkar et al. 2004; Chardon et al. 2004). The latter authors studied the genetic architecture of flowering time (FT) in maize and identified six genome regions with a major effect on earliness.

The purpose of this paper is to propose an overview of the genome regions involved in the control of wheat earliness, and to refine the positions of their related QTL. A first step consisted in collecting earliness QTL data available in the literature and then to use the empirical overview developed by Chardon et al. (2004) to obtain an empirical map of the genome regions involved in earliness control. Then a second step consisted in using a meta-analysis to combine the QTL data obtained from independent studies. The criterion proposed by Goffinet and Gerber (2000) was used to test the presence of one or several QTL in the same region of a linkage group. New criteria are also proposed to investigate the quality of QTL projection.

Materials and methods

We developed a three-step strategy to characterize the QTL involved in earliness control in bread wheat. The first point consisted in the collection and characterization of data. We therefore reviewed the bibliography and characterized different earliness experiments. Secondly, we prepared the data for a further meta-QTL analysis: genetic maps from the different studies, together with QTL, were projected on a consensus map. The third point consisted in summarizing the QTL data using a QTL empirical overview and a meta-QTL analysis. The reliability of the results thus obtained was evaluated using quality criteria.

Bibliographical review

Fifteen published and two unpublished studies were found to present earliness QTL and mapping data. Only 13 provided sufficient information on mapping and QTL characteristics to carry out map projections and QTL meta-analysis. The references are listed in Table 1. The studies which could not be used were those by Worland (1996), Kato et al. (1999, 2002) and Sourdille et al. (2000). In addition, alleles at the suspected *Vrn_A1* (Kato et al. 1998) and the suspected *Ppd_D1* (unpublished study) genes were phenotypically identified in segregating populations by registering earliness in specific experiment. These two phenotypic markers were mapped and compared with projected QTL locations.

Earliness traits

In the different papers reviewed, earliness was often assessed by registering the heading date (HD) and/or FT for conventional autumn or winter sowing dates. HD and FT were factors of variation for the agronomic traits studied. By contrast, authors who specifically investigated earliness applied a particular design to measure one or more of the three earliness components: PS, VR and IE. All these earliness QTL were included in the analysis, but identified as HD or FT, PS, VR and IE QTL.

Photoperiod sensitivity is classically estimated as a deviation, either of the flag-leaf unfolding date (FLUD) (Shindo et al. 2003), or the first headed spike date (FHSD) (Hanocq et al. 2003) or the HD (Sourdille et al. 2003, Hanocq et al. 2003, 2004), under vernalized-long day condition and vernalized-short day condition. VR is estimated as either the HD or FT for unvernalized plants grown under a non-limiting photoperiod and temperature (Galiba et al. 1995; Kato et al. 1998; Leonova et al. 2003), or as a deviation of the FLUD (Shindo et al. 2002, 2003) or HD (Toth et al. 2003; Hanocq et al. 2003, 2004) under vernalized and unvernalized treatments. IE is estimated from the FLUD (Shindo et al. 2002, 2003), HD (Sourdille et al. 2003; Hanocq et al. 2003, 2004; Toth et al. 2003) or FHSD (Kato et al. 1999) under vernalized conditions when the photoperiod is not limiting.

Table 1 Studies proposing earliness QTL

First author	Year	Genetic material	Pop size	Map density (cM)	Chromosome																						Total number of QTL per study
					1			2			**3**			4			**5**			6			**7**				
					A	**B**	**D**	A	B	D	**A**	**B**	**D**	A	B	D	**A**	**B**	**D**	A	B	D	**A**	**B**	**D**	
1 Börner	2002	ITMI population: Opata 85 × W7984	114	12					1 (3)	3 (7)				1	1				**1 (7)**	1 (2)					**1 (2)**	9 (23)
2 Charmet	Personal communication	Eurêka × Renan	152	12						2 (3)				1												3 (4)
3 Galiba	1995	CS (T. spelta 5A) × CS (Cheyenne 5A)	119	15	–	–	–	–	–	–	–	–	–	–	–	–	**2**	–	–	–	–	–	–	–	–	2
4 Gervais	2003	Renan × Récital	194	17					1 (3)																	1 (3)
5 Hanocq	2003	Arche × Récital	241	14				1	4 (21)	4 (23)				2 (4)			**1 (9)**	**2**		1	1					16 (62)
6 Hanocq	2004	Renan × Récital	194	13					4 (6)	2 (5)							**2 (3)**	**2**	**1**			1 (2)	**1**		**2**	15 (22)
7 Kulwal	2003	ITMI population: Opata 85 × W7984	110	10			**1**			3				1												5
8 Le Gouis	Personal communication	Apache × Ornicar	189	10		**2**				1 (6)					1 (6)		**1**	**2 (3)**					**1 (6)**			8 (24)
9 Leonova	2003	Diamant (Mironovskaya 808 5A) xBezostaya 1	160	14	–	–	–	–	–	–	–	–	–	–	–	–	–	**1**	–	–	–	–	–	–	–	1
10 Shindo	2002	RILWA-1 population: T. monoc. L. (acc. KT3-5), xT. beotic. (acc. KT1-1)	115	13							***2***						**3**									5
11 Shindo	2003	CS × T. Spelta var. Duhamelianum KT19-1	66	17					*5*								**1**	**5**	**1**							12
12 Sourdille	2003	Courtot × CS	187	19					2						1		**2**		**1**					**3**	**1**	10
13 Toth	2003	CS × CS (Cheyenne 5B)	61	12	–	–	–	–	–	–	–	–	–	–	–	–	–	**4**	–	–	–	–	–	–	–	4
		Hobbit Sib x Hobbit Sib(CS 5BL)	76	5																						
Total number of QTL per chromosome					**0**	**2**	**1**	1	17 (40)	15 (47)	**2**	**0**	**0**	5 (7)	3 (8)	0	**12 (21)**	**16 (17)**	**4 (10)**	2 (3)	1	1 (2)	**2 (7)**	**3**	**4 (5)**	Total: 91 (177)
Total number of QTL per group						**3**			33 (88)			**2**			8 (15)			**32 (48)**			4 (6)			**9 (15)**		

CS Chinese Spring,
(): number of initial QTL before preliminary meta-analysis, –: chromosome not studied by the authors; *Italic script* chromosome that could not be projected on the reference map

Characteristics of earliness studies

The genetic materials, population sizes and average distances between markers are presented in Table 1. QTL mapping population sizes ranged from 61 (Toth et al. 2003) to 241 lines (Hanocq et al. 2003). Coverage of the genome was quite similar across the genetic maps and the average distance between markers was 13 cM.

Three studies investigated the *Vrn* genes series controlling VR and located on group 5 chromosomes (Galiba et al. 1995 on 5A; Leonova et al. 2003; Toth et al. 2003 on 5B). They thus only focused on group 5 chromosomes and used the mapping populations obtained with a substituted parent derived from cytological studies based on the work by Sears (1953).

Overall, the 13 studies, in which QTL were projected, proposed 177 earliness QTL: 86 were HD QTL, 21 were FT QTL, 15 were PS QTL, 29 were VR QTL and 22 were IE QTL. In addition, four of the 177 QTL concerned frost resistance (FR) or winter hardiness (WH) QTL. The studies investigating the whole genome detected between 3 (Gervais et al. 2003) and 62 (Hanocq et al. 2003) individual QTL. Gervais et al. (2003) published QTL for mean earliness over 3 years, whereas the analysis carried out by Hanocq et al. (2003) collated earliness QTL detected in several experiments. This illustrates the fact that the information provided by different authors was highly heterogeneous.

Map and QTL projections

Map projection issues

The projection of original genetic maps onto a reference map is a means of comparing the QTL detected using different populations. We therefore considered Somers's bread wheat consensus map (Somers et al. 2004) as the reference map. It contains 1,235 microsatellite markers for a total length of 2,569 cM giving thus an average distance between markers of 2.2 cM. Somers's 4B chromosome had to be reverted because the markers were in a reverse order when compared with the maps used by all other authors.

The MapInspect software (Van Berloo 1999) was used to graphically assess the quality of projections. Possible discrepancies induced by ''multiband'' markers were carefully examined as they could frequently cause major inversions to the order of the common marker. Such discrepancies were filtered out by discarding inconsistent loci. With the exception of very closely linked markers, inverted markers were automatically discarded from the projection process using the appropriate BioMercator v2.0 option (Arcade et al. 2004). In the case of pairwise inversions where the marker interval was smaller than 1 cM, only one of the two markers was manually and arbitrarily removed in order to retain a maximum number of common markers. Such inversions were quite frequent, and mainly due to the limited size of some populations. In addition, for populations such as Arche × Récital (Hanocq et al. 2003) and Apache × Ornicar (Le Gouis J, personal communication), some parts of the map could not be linked to the reference map, probably because of suspected translocations.

If there were insufficient common markers in the original map (Galiba et al. 1995; Börner et al. 2002; Shindo et al. 2002, 2003) and the Somers's map, a direct projection was not possible. In such cases, we considered the map developed by Röder et al. (1998) or the current ITMI map (Leroy P, personal communication) as transitional maps. The homothetic projection principle and use of intermediate maps are illustrated in Fig. 1.

For convenience, Somers's map was preferred to the ITMI map, from which it had been directly derived. On the one hand, the ITMI map would have enabled the determination of more common markers between

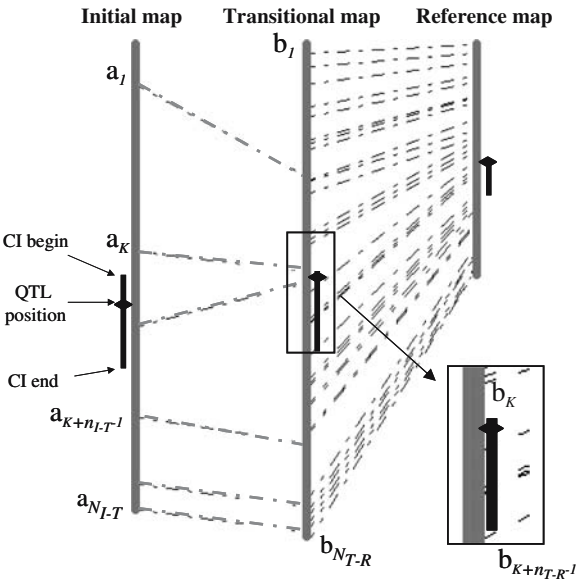

Fig. 1 Principle of QTL projection from an initial map to a reference map via a transitional map. *Heavy type bar* right and left QTL confidence interval (CI) ends; *heavy type mark* QTL position

maps because of its very large number of markers, but on the other hand, projections would have been very tedious in many cases, due to the frequent pairwise inversions between very closely linked markers.

QTL projection issues

QTL were projected onto the reference map using the BioMercator v2.0 software (Arcade et al. 2004). First, the initial QTL and reference maps were linked through their common markers, which were then used to assess a homothetic function. This function enables computation of the most likely position and the confidence interval (CI) of the projected QTL on the reference map (Fig. 1). To address possible heterogeneity in definition of CI across studies, whenever possible, initial QTL CI values were replaced by a 95% CI, estimated using the approach described by Darvasi and Soller (1997):

$$\mathrm{CI} = \frac{530}{NxR^2}, \quad (1)$$

where N is the size of the population and R^2 the proportion of variance explained by the QTL. This approach enabled the calculation of a CI when one was not published, and to assess the CI using the same method for each QTL and study. However, we used the published CI values for QTL from Galiba et al. (1995), Börner et al. (2002) and Leonova et al. (2003) because their R^2 values were not documented.

QTL empirical overview

The empirical overview approach proposed by Chardon et al. (2004) was used to visualize through a simple way the importance of a genome region in the earliness traits control. For convenience, a relative probability level (RPL) was defined every 0.5 cM as the ratio between the density function computed as indicated by Chardon et al. (2004), and the density called ''average value'' by these authors. For a given genome region, the higher the RPL, the higher the probability that it is involved in the control of earliness traits.

Consensus QTL

The meta-analysis approach (Goffinet and Gerber 2000) was used to cluster the individual QTL detected during independent experiments and located in a same genome region. According to Goffinet and Gerber (2000), for a same trait, were considered as independent any experiments carried out in different plant populations, at different locations or under different environmental conditions. It has to be noticed that when HD and FT QTL were present in the same genome region for the same experiment, they could not be considered as independent, as required for meta-analysis. In such cases, only HD QTL was considered. More generally, frequently, several QTL were detected on the same chromosome for the same trait and during the same experiment. Checks were thus made that such QTL were not pooled under the meta-analysis. These consensus QTL obtained from the meta-analysis were referred to as meta-QTL (MQTL). Computations were performed using BioMercator v2.0 software (Arcade et al. 2004). For n individual QTL, the software tests the most likely assumption between 1, 2, 3, 4 and n underlying QTL. Decision rules are based on an Akaike-type criterion. When the n-model was the most likely model, the meta-analysis was performed again, but on subsets of the QTL. These subsets were considered on the basis of the ''progressive'' clustering of individual QTL from the 4-model to the 1-model. The meta-analysis approach made it possible to refine the position of the QTL involved in earliness control, because MQTL CIs were reduced when compared to the initial ones.

Quality aspects

The reliability of meta-analysis results depends firstly on the accuracy of initial QTL parameter estimates and secondly on map and QTL projection quality. No quality criteria are delivered by the BioMercator software. For this reason, different criteria are proposed in this paper to assess quality aspects related to both initial QTL properties and the projection.

In terms of initial QTL parameters

Independently of initial QTL CI that are sometimes underestimated, a distal QTL position may impair accuracy if the true QTL position lies outside the available genetic map. In other words, such a QTL may be found at a different site on a more extended map. Therefore, after estimating the CI using Darvasi's formula (equation 1) for each QTL, checks were made that the CI was partially or completely included within the initial genetic map.

With respect to projection characteristics

A projection from an initial map to a reference map is based on common markers; both map and QTL pro-

jection quality are dependent on them. We therefore studied the number and density of these markers as well as their relative distribution throughout the initial and reference maps in the QTL region. Homothetic coefficient values and their variations in the chromosome are dependent on those parameters. Moreover, for a given chromosome, common markers are not necessary scattered throughout the entire genetic map, so that the linked region of a given linkage group, i.e. the region between the two extreme common markers, is often shorter than the genetic map. In such cases, QTL CI may lie partially or completely outside the linked region.

Five variables were calculated to assess QTL projection quality for each QTL: the percentage of QTL CI included in the linked region, N_m (the number of common markers characterizing a QTL CI region i.e. within and flanking it), LMD (local map density) which is computed as the local average distance on the N_m markers on the projected map, MGS (maximum gap size), or the size of the largest interval between adjacent markers when considering the Nm markers and WSD_{100} (the weighted standard deviation standardized to 100 cM) which evaluate the heterogeneity in homothetic coefficients for intervals within and flanking a QTL CI region. N_m, MGS, LMD and WSD_{100} are described in Table 2; they are available including if a transitional map is used. In such cases, given the high concordance between the transitional and reference maps, the quality of the projection from transitional map was not considered as a limiting factor.

Results

A total of 91 QTL or MQTL from 13 studies covered almost the whole genome.

Preliminary within study meta-analysis

As mentioned above, the means of presenting QTL detection results varied from one study to another. In the case of multi-environmental experiments, for a same trait, it is possible to summarize data over environments before QTL detection, but it is also possible to realize one QTL detection per environment and to present as many QTL detection results as environments without pooling. Since the QTL meta-analysis model of Goffinet and Gerber (2000) requires independent QTL analyses as input, data from multi-environmental experiments that present as many QTL detection results as environments must be previously investigated to identify which QTL are distinct.

So, before doing the overall meta-analysis including all the studies, if necessary, we did within study preliminary meta-analysis for clustering QTL data over environments. This preliminary meta-analysis was performed on the two unpublished studies referring to the Eurêka × Renan (2D, 4A chromosomes) (Charmet G, personal communication) and Apache × Ornicar (2D, 4B, 5B, 7A) (Le Gouis J, personal communication) populations and on the studies published by Börner et al. (2002) (2D, 5D, 7D), Gervais et al. (2003) (2B), Hanocq et al. (2003) (2B, 2D, 4A, 5A), Hanocq et al. (2004) (2B, 2D, 5A, 6D) and Kulwal et al. (2003) (2D). For studies with QTL relative to several independent traits, one within study preliminary meta-analysis was performed on each trait.

The above studies 1, 2, 4, 5, 6, and 8 (Table 1) presented results in considerable detail. The preliminary meta-analysis reduced the number of QTL from 138 to 52. Overall, of the 177 QTL reported in the original studies, 91 QTL (or preliminary MQTL) were retained for map projections; 43 were HD or FT QTL registered for conventional sowing dates, 12 were PS QTL, 14 were VR QTL, 18 were IE QTL, 3 were FR or WH QTL, and 1 corresponded to earliness under short-day condition.

Before doing the overall meta-analysis of the 91 QTL or preliminary MQTL across all the studies, for each preliminary MQTL the position considered was the position obtained by the preliminary analysis and a Darvasi CI based on the mean initial R^2 values of the corresponding initial QTL was re-calculated.

Quality criteria demonstrated disparate situations regarding map and QTL projections

All genome regions containing at least one QTL could be projected on Somers's map, except for chromosome 3A in study 10 and chromosome 2B in study 11. In these two regions, only one marker was common to the two maps. The CI of eight QTL lay completely outside the linked region: on chromosomes 2B, 5B and 6A (study 5), on chromosome 7D (study 6), on chromosomes 5B (study 11) and on 2B and 4B (study 12). For six QTL, less than half of the CI was included in the linked region: on chromosomes 5A (studies 3, 11), 4A (study 5) and 5D (study 6). In addition, six QTL were located at a completely distal position on the initial genetic map (study 5 for 2B, 4A and 5A, study 11 for 2B and study 13 for 5B).

The average number of common markers related to QTL CI (Nm) in all studies was 2.8. This value ranged from 1, for a QTL CI lying out of the ''extended QTL CI region'', to 7. Only 19% of QTL CI comprised more

Table 2 Criteria used for measuring QTL projection quality

Criterion	For a direct projection from the initial to the reference map	For a projection from the initial to the reference map through a transitional map
N_m	$n_{I\text{-}R}$	$n_{I\text{-}T}$
MGS	$\max_{i=K \text{ to } (K+n_{I-R}-2)} d''(a_i, a_{i+1})$	$\max_{i=K \text{ to } (K+n_{I-T}-2)} (d'(a_i, a_{i+1}))xH_{T-R}$ with $H_{T-R} = {d''(b_1, b_{N_{T-R}})}/{d'(b_1, b_{N_{T-R}})}$
LMD	${d''(a_K, a_{K+n_{I-R}-1})}/{n_{I-R}}$	${d'(a_K, a_{K+n_{I-T}-1})}/{n_{I-T}}$ $x\ H_{T-R}$
WSD_{100}	$\sqrt{\sum_{i=K-1}^{K+n_{I-R}-1} \left(\frac{d(a_i,a_{i+1})}{d(a_{K-1},a_{K+n_{I-R}})} x (H_i - \bar{H})^2\right)}$ with $H_i = {d''(a_i, a_{i+1})}/{d(a_i, a_{i+1})}$ and $\bar{H} = {d''(a_{K-1}, a_{K+n_{I-R}})}/{d(a_{K-1}, a_{K+n_{I-R}})}$	$\sqrt{\sum_{i=K-1}^{K+n_{I-R}-1} \left(\frac{d(a_i,a_{i+1})}{d(a_{K-1},a_{K+n_{I-R}})} x (H_i x H_{T-R} - \bar{H})^2\right)}$ with $H_i = {d'(a_i, a_{i+1})}/{d(a_i, a_{i+1})}$ and $\bar{H} = {d'(a_{K-1}, a_{K+n_{I-R}})}/{d(a_{K-1}, a_{K+n_{I-R}})} xH_{T-R}$

N_m number of common markers characterizing a QTL CI region, *MGS* maximum gap size, *LMD* local map density, WSD_{100} weighted standard deviation standardized to 100 cM

$n_{I\text{-}R}$ and $n_{I\text{-}T}$ are the number of common markers characterizing a QTL CI region (i.e. within and flanking it) between the initial and reference maps, and between the initial and transitional maps, respectively

a_i and b_i are the $i^{ième}$ common markers between maps when projecting from the initial map and when projecting from the transitional map, respectively

$d(a_i,a_j)$, $d'(a_i,a_j)$ and $d''(a_i,a_j)$ are the genetic distance (cM) between the markers a_i and a_j when measuring on the initial, transitional and reference maps, respectively

K is the marker number of the first common markers flanking the QTL CI region

$H_{T\text{-}R}$ is the overall homothetic coefficient between the transitional and reference maps

$N_{T\text{-}R}$ is the total number of common markers between the transitional and reference maps

H_i is the homothetic coefficient relative to the projection of the interval I_i flanked by the common markers i and $i + 1$

$\bar{H}$ is the overall homothetic coefficient relative to the extended QTL CI region comprise between the common markers $K\text{-}1$ and $K + n_{I\text{-}R}$

than three common markers. An average of 1.8 common markers was found per 10 cM in the projected QTL CI. LMD criterion values ranged from 1.7 to 92.0 cM, with a mean of 23.0. MGS values ranged from 3.0 to 92.0, with a mean of 27.4. MGS exceeded an arbitrary value of 50 cM in seven QTL, four located on chromosome 5A (studies 6, 10, 11 and 12), two on 2D (study 2) and the last on 7A (study 6). WSD_{100} values ranged from 0.03 to 2.02 for the 2D and 4B QTL in study 8, respectively. The two QTL on 2D in study 2 were also projected with a high WSD_{100} (1.89). The distribution of WSD_{100} values (Fig. 2) revealed extremely high values for these last three QTL only. Overall, WSD_{100} values exceeded an arbitrary threshold of 0.7 (fixed on the basis of the distribution in Fig. 2) for ten additional QTL located on chromosomes 4A (studies 6 and 7), 5B (studies 11 and 13) and 6A (study 1).

Maps and QTL projections

The 91 remaining QTL referenced in the 13 studies were spread over almost the entire genome (Table 1). The distribution of QTL in the reference Somers's map can be visualized by using the empirical overview approach (Fig. 3). In 13 cases, the RPL exceeded the arbitrary level of five (fixed by Chardon et al. 2004). In four cases, it exceeded ten: chromosomes 2B (18.8 at position 45.5 cM on Somers's 2B map), 2D (22.3 at position 40.7 cM), 4A (13.3 at position 49.0 cM) and 5A (13.2 at position 106.5 cM). Four chromosomes (2B, 2D, 5A, 5B) exhibited more than ten initial QTL detected in at least five studies. In chromosome 2B, RPL curve revealed a single main peak. Several peaks were observed for chromosomes 2D, 5A and 5B. These peaks were very close together in chromosome 2D, but in 5A and 5B, the peaks were clearly distinct from each other, each corresponding to several clusters of QTL.

There was a significant imbalance in QTL breakdown between the seven groups of chromosomes. Indeed, without considering specific chromosome studies (i.e. studies 3, 9 and 13), groups 2 and 5 together accounted for 68% of QTL, whereas groups 1, 3 and 4 together accounted for only 11%. Groups 4 and 7 each contained about 10% of QTL. However, the differences observed between the three genomes: A (26%),

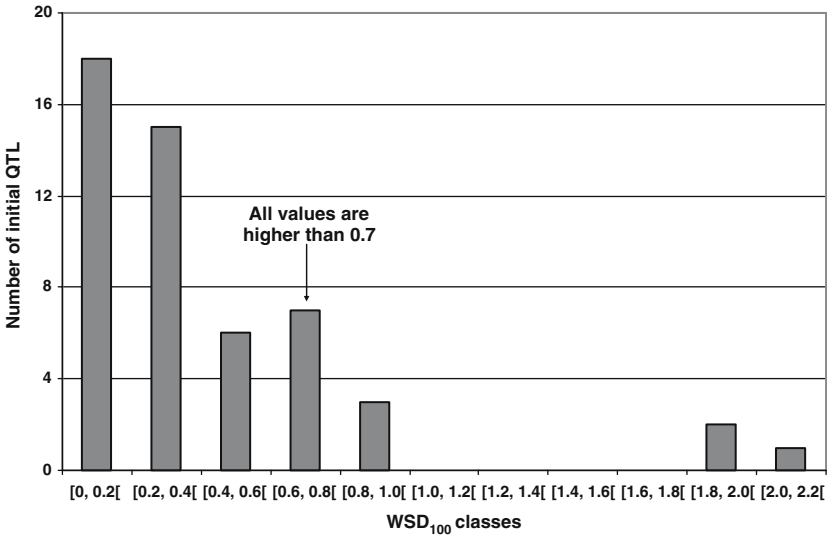

Fig. 2 Distribution of WSD_{100} criterion values concerning the initial QTL involved in meta-QTL

B (44%) and D (30%), for which genome lengths were respectively 871, 847 and 778 cM, were not statistically significant. A difference between genomes was observed for group 2 and to a lesser extent for group 5. For instance, only one QTL was detected on 2A versus 17 and 15 on 2B and 2D, respectively. Each 2B, 2D, 5A and 5B chromosome contained more than 10 QTL, but otherwise no chromosomes contained more than five QTL, and no QTL were detected on chromosomes 1A, 3B, 3D and 4D.

Among the HD, FT and PS QTL, 44% were located on group 2 chromosomes, whereas the others were almost equally distributed between groups 4, 5 and 7. Groups of chromosomes 2 and 5 shared the majority of IE QTL. Seventy-nine percent of VR QTL were located on group 5.

Meta-analysis results

Of the 84 QTL that could be projected on the Somers's map, only four were alone in their linkage group (Fig. 3), so 79 were candidates for aggregation in the so-called MQTL using a meta-analysis approach. Meta-analysis resulted in 18 MQTL and 12 remaining individual QTL. The most accurate MQTL were located on 2D, 4B, 5A and 5B, with CI values of 0.6, 1.1, 3.2 and 4.2 cM, respectively. With respect to the reduction in the length from mean initial to meta-QTL CI, the gain in accuracy ranged from 1.4 to 32.8. As a general tendency, the gain increased with the number of initial QTL. Nevertheless, the very high values of 12.7, 32.8 and 22.8 for the MQTL 4, 5 and 8, respectively (Table 3), were due to very accurate initial QTL. On chromosomes 5A and 5B, the distribution of a large number of QTL (12 and 16, respectively) revealed a clear clustering of QTL. On 2B and 2D (with 12 and 15 QTL, respectively), they were more evenly spread along the chromosome. The maximum number of original QTL pooled together by MQTL was eight (on 5B—MQTL 12). It was observed that meta-analysis often enabled the aggregation of two individual QTL with poor original accuracy, such as in 2B (MQTL 3), 5B (MQTL 11), 5D, 7A, 7B and 7D.

When focusing on 2B, three MQTL could be observed (Table 3). The first (MQTL 1 in Fig. 3), positioned at 38.5 cM on the 2B chromosome of the Somers's map, was derived from the three original HD QTL and from one of the three original IE QTL. The second MQTL (MQTL 2), located at 46.8 cM aggregated the two PS QTL, the two FT QTL and the two remaining IE QTL. These two MQTL were proposed by the BioMercator software with a modified Akaike criterion only slightly inferior (66.52) to the Akaike criterion (69.83) corresponding to a single MQTL positioned at 41.53 cM and containing the previous two MQTL. The third MQTL (MQTL 3) was derived from the two VR QTL located on 2B. It was positioned at 77.0 cM and had a relatively broad CI of 13 cM.

On chromosome 2D (Table 3), most of the 15 QTL originating from six studies were HD QTL. Two QTL (HD_1—30.6 cM and HD_7—57.8 cM) were clearly sited at locus different from the other 13 (Fig. 4) and were not aggregated into a MQTL. The 13 remaining QTL were clustered in three MQTL. The first (MQTL 4), located at the 37.6 cM position, contained four initial QTL: three HD QTL and one IE QTL. The second MQTL (MQTL 6), located at 46.1 cM, was derived from only two original IE and HD QTL from study 5 performed on the Arche × Récital population (Hanocq et al. 2003). These two original QTL were

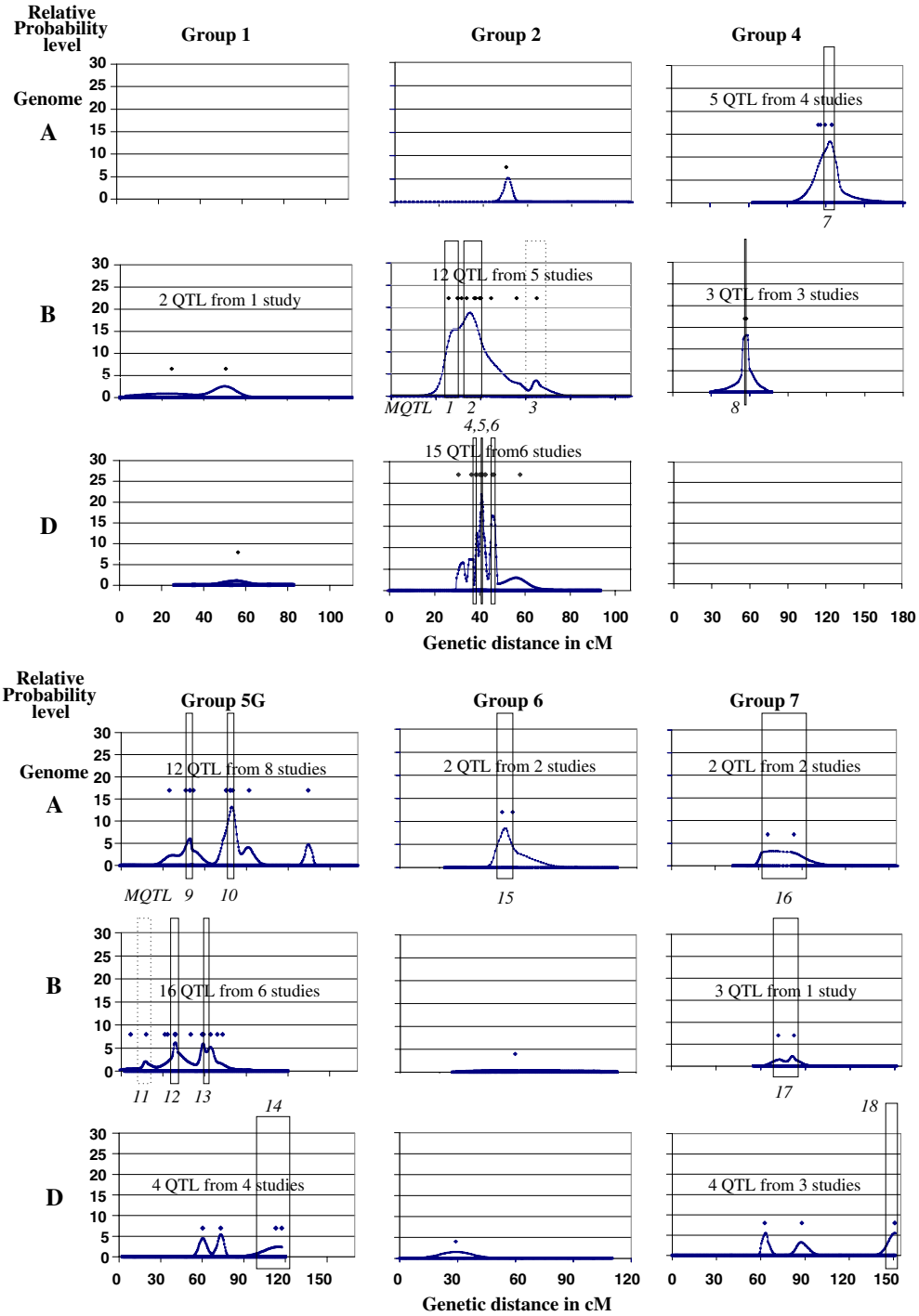

Fig. 3 Initial QTL, empirical overview and meta-QTL results concerning earliness QTL in bread wheat. *Points* projected initial QTL positions. *Curves* relative probability level (RPL) corresponding to the density of the projected QTL/density of the uniform distribution ratio. *Rectangle* confidence interval area of the meta-QTL. *Dotted rectangle* meta-QTL not confirmed after excluding initial QTL due to projection quality aspects. *Reference chromosomes for the homoeology approach* 1B, 2D, 4A, 5D, 6D and 7D. *Thick horizontal bar* on the *abscissa* axis: initial chromosome length

both very accurate. Globally, the four original QTL derived from the Arche × Récital population displayed narrow CI values. MQTL 5 and 6 were close to each other, but when they were clustered in a single MQTL the Akaike criterion increased from 64 to 131.5. The third MQTL (MQTL 5), located at 41.1 cM, contained the remaining seven QTL, all of them HD or FT QTL except for one PS QTL. It can be seen from Fig. 4 that the position of MQTL 5 was largely determined by the single initial but very accurate Arche × Récital PS QTL. In addition, the phenotypic *Ppd-D1* marker developed during an unpublished study on a Mercia × Mercia (Ciano 67—2D) population was precisely projected at a position (39.7 cM) very close to that of these last QTL. The three 2D MQTL were very accurate with CI between 0.6 and 1.5.

On chromosome 4A, five QTL originating from four studies (1, 2, 5 and 7) were included in MQTL 7

Table 3 Characteristics of meta-QTL (MQTL)

Chrom	Meta-QTL	Position on Somers's map	CI begin	CI end	Flanking markers of the position	Number of initial QTL	Number of initial study	Mean initial R^2	Coefficient of reduction in length from mean initial to meta-QTL CI	Candidate trait	Candidate major gene
2B	1	38.5	35.9	41.0	wmc597–wmc257	4	3	21.1	2.9	**HD**/(IE)	*Ppd-B1?*
	2	46.8	43.5	50.1	wmc770–gwm148	6	5	12.5	3.4	**FT/PS/IE**	*Ppd-B1?*
	3	77	70.5	83.5	wmc441–wmc500	2	2	6.7	2.1	**VR**	
2D	4	37.6	36.8	38.3	wmc470–gwm484	4	3	30.3	12.7	**HD**/(IE)	
	5	41.1	40.8	41.4	gwm484–wmc453	7	5	38.9	32.8	**HD**/(PS)	*Ppd-D1*
	6	46.1	45.5	46.6	wmc453–barc168	2	1	22.6	2.7	**HD/IE**	
4A	7	48.2	45.8	50.6	gwm565–gwm494	5	4	8.6	4.4	**HD**/(PS)	
4B	8	24.3	23.8	24.9	wmc310–gwm251	3	3	6.0	22.8	**HD**/(PS)	
5A	9	76.5	72.6	80.3	gwm639–gwm617	4	4	10.3	2.8	**HD**/(PS)	
	10	106.5	104.9	108.1	cfa2155–cfa2141	5	4	17.4	4.5	**VR**/(HD)	*Vrn-A1*
5B	11	38.5	30.0	46.9	gwm234–wmc149	2	2	14.7	2.5	**HD/IE**	
	12	76.5	71.6	81.4	gwm499–gwm639	8	5	10.9	5.0	**IE**/(HD-VR)	
	13	113.4	111.3	115.5	wmc326–wmc75	6	3	21.0	5.8	**VR**/(HD-PS)	*Vrn-B1*
5D	14	115	101.0	129.1	gwm565–gwm272	2	2	7.7	1.4	**VR**	
6A	15	25.6	23.4	27.9	barc23–wmc182	2	2	11.3	2.1	**PS/Wh**	
7A	16	57.7	48.4	67.1	wmc83–wmc405	2	2	8.1	1.5	**HD/IE**	
7B	17	45	34.5	55.5	gwm537–gwm68	3	1	8.4	1.4	**HD**/(IE)	
7D	18	150.9	144.9	156.9	wmc166–wmc14	2	2	6.9	1.4	**HD**	

Position and CI are expressed in cM. Candidate traits studied were heading date (*HD*); flowering time (*FT*), photoperiod sensitivity (*PS*), intrinsic earliness (*IE*), vernalization requirement (*VR*), winter hardiness (*Wh*). In *bold type*: majority trait for the initial QTL included in the MQTL

Chrom chromosome, *CI* confidence interval

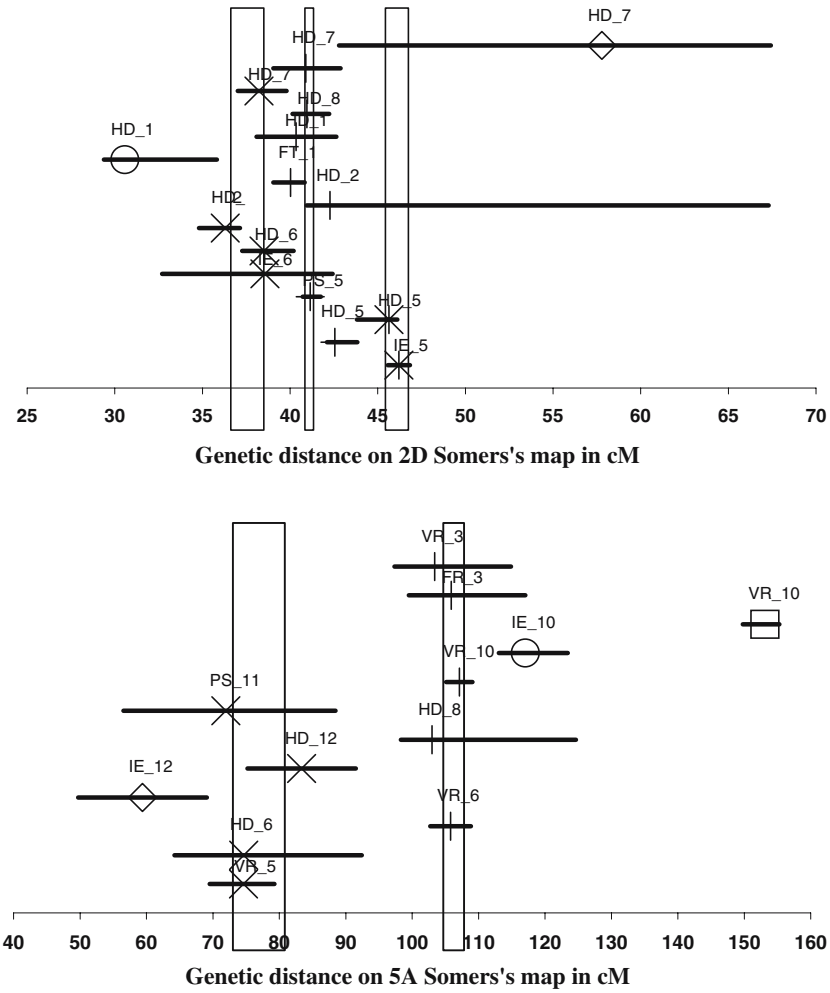

Fig. 4 Illustration of meta-analysis of chromosomes 2D and 5A. *Rectangle* confidence intervals of the meta-QTL. Projected QTL represented with same symbols (*indicating position*) belong to the same meta-QTL. *Horizontal bars* projected QTL CI. *VR* vernalization requirement, *FR* frost resistance, *IE* intrinsic earliness, *HD* heading date, *FT* flowering time QTL

located at 48.2 cM. Four of these initial QTL (detected in four studies) were HD QTL; the fifth was a PS QTL.

On chromosome 4B, three QTL (two HD QTL and one PS QTL), detected in three studies, were pooled in the MQTL 8 located at 24.3 cM with a CI of 1.1 cM. The three initial QTL were all projected within a very close genome region of 1.2 cM. R^2 values for these individual QTL did not exceed 6.3%, except for the HD QTL from study 1, whose R^2 value was not documented.

On chromosome 5A, unlike chromosomes of the group 2, individual QTL could clearly be pooled in two distinct clusters: the CI of the initial QTL from these two distinct clusters did not overlap (Fig. 4). Two MQTL were observed at positions 76.5 cM (MQTL 9) and 106.5 cM (MQTL 10). These MQTL contained four and five initial QTL, respectively. The CI of the IE QTL from Shindo et al. (2002) (Fig. 4) largely overlapped the CI of three of these last five QTL; nevertheless it was not included in the MQTL. An IE QTL, which was not included in the meta-analysis because of insufficient data, was detected approximately in this region by Kato et al. (1999). MQTL 9 derived essentially from individual HD or PS QTL (except one VR QTL from study 5) and MQTL 10 from individual VR QTL (except one HD QTL from study 8). The phenotypic *Vrn-A1* marker described by Kato et al. (1998) was projected at a similar position (107.1) as the VR MQTL 10 (106.5 cM). Three individual QTL were not pooled by the meta-analysis.

On chromosome 5B, it has been identified three MQTL (MQTL 11 to 13), located at 38.5 cM (CI 16.9 cM), 76.5 cM (9.8 cM) and 113.4 cM (4.2 cM), and clustering three, eight and six individual QTL, respectively. Half of the individual QTL pooled in MQTL 12 were IE QTL, whereas half of the individual QTL in MQTL 13 were VR QTL.

One MQTL was computed for each of the 5D, 6A, 7A, 7B and 7D chromosomes. They resulted from the aggregation of two individual QTL and had quite a broad CI ranging from 12.1 cM for MQTL 18 on 7D to 18.7 cM for MQTL 16 on 7A. In addition, on chromosomes 5D and 7D, the MQTL were at a very distal position.

Changes to QTL meta-analysis results when quality aspects were taken into account

A second overall meta-analysis was performed after excluding QTL suspected of having an uncertain initial position or being projected with insufficient accuracy on the basis of quality criteria values. Thus, the six QTL located at one extremity of their initial chromosome map and the 10 QTL with a WSD_{100} criterion higher than 0.7 were excluded from the analysis. Those 16 QTL corresponded to five QTL from study 5 (two on 2B—MQTL 1 and 3, two on 4A—MQTL 7 and one on 5A—MQTL 9), two QTL from study 2 (on 2D—MQTL 4 and 5), one QTL from study 7 (on 4A—MQTL 7), one QTL from study 8 (on 4B—MQTL 8), four QTL from study 11 and three QTL from study 13 (both on 5B, MQTL 11 to 13). For chromosome 5B, seven QTL (from two studies) out of the initial 16 QTL were removed. More generally, the quality criteria highlighted the fact that few entire chromosomes were projected with limited accuracy: 4A from study 5, 2D from study 2, 5B from study 11 and study 13 (Cheyenne population). This might also have been due to the fact that some initial genetic maps were of limited length (study 5).

When compared to the meta-analysis including the entire set of QTL, removal of the 16 QTL referred to the above had three consequences: (i) Firstly, on chromosomes 2D (MQTL 5), 4A (MQTL 7) and 4B (MQTL 8), the exclusion of six initial QTL had almost no effect on MQTL location: the initial QTL removed had very poor accuracy and thus little incidence in determining MQTL characteristics. Nevertheless, MQTL CI were sometimes increased by removing QTL, because of the smaller number of initial QTL aggregated within each MQTL. (ii) Secondly, the exclusion of QTL led to a clearer segregation of traits. On 5A, MQTL 9 was no longer a mixture of HD and VR QTL, the latter being removed. (iii) Thirdly, the removal of initial QTL resulted in a deletion of MQTL (3 and 11). The remaining QTL that had initially been included in these two MQTL were either aggregated with another MQTL (e.g. 2B) or remained unpooled (e.g. 5B).

Homoeology aspects: groups 2, 5 and 7 recorded homoeologous MQTL

Investigations relative to the homoeology of QTL and MQTL between genomes A, B and D were developed by projecting each chromosome from each group onto one of the three genomes, depending on the ease of determining common markers. As shown in Fig. 3, chromosomes 1B, 2D, 4A, 5D, 6D and 7D were considered as references for each of their homoeology groups. Links between within-group genetic maps were often possible through use of the ITMI map and multilocus markers. Nevertheless, in group 4, the projection was presented on the 4A ITMI map because chromosomes 4A and 4B in the Somers's map were almost not overlapping. It is thus clear that the MQTL for these two chromosomes could not be determined as being homoeologous.

For group 2 chromosomes, the MQTL 2 and 4 appeared to be homoeologous. In group 5, homoeology was observed between MQTL 9 and 12 of 5A and 5B, respectively. They controlled both HD/IE traits. However, in the same chromosomes, the two VR MQTL 10 and 13 were at a distance of 13 cM when projected on 5D. In group 7, homoeology was observed for the two HD/IE MQTL located on 7A and 7B.

Discussion

QTL data compilation showed that all chromosome groups were involved in the genetic control of earliness in bread wheat. Only four chromosomes exhibited no QTL. The number of QTL per chromosome ranged from 0 to 16. Groups 2 and 5 were key groups for earliness control. Groups 4 and 7 had a secondary but consistent incidence. Groups 1 and 3 had a highly limited incidence. We discuss these genetic and agronomic results below.

The meta-analysis methodology proposed by Goffinet and Gerber (2000) was applied to QTL studies. It resulted in the detection of several meta-QTL, and showed that this method was a very powerful tool which could refine QTL position and accuracy. However, it is necessary to consider the accuracy and reliability of input data concomitantly, applying the quality criteria proposed in this paper. These methodological aspects are also discussed below.

The genetic control of earliness and its components involves not only the major genes of the Ppd and Vrn families but also other genome regions in groups 4 and 7 with lesser effects

Cytogenetic studies have shown that groups 2 and 5 contain the major genes controlling PS (*Ppd* series) (Welsh et al. 1973; Law et al. 1978) and VR (*Vrn* series) (Law et al. 1976; Maystrenko 1980), respectively. However, a meta-analysis approach helped to consider these global results in detail. We therefore compared

the data in the literature with the results of the QTL meta-analysis. *Ppd-D1*, *Vrn-A1 and Vrn-B1* appeared to correspond to MQTL 5 (Position 41.1 on Somers's 2D map), MQTL 10 (106.5) and MQTL 13 (113.4), respectively (Table 3). MQTL 1 (38.5) and MQTL 2 (46.8) appeared to correspond to *Ppd-B1*, and a single MQTL (41.5) containing both MQTL 1 and 2 was also highly probable. On chromosome 5D, the VR MQTL 14 was not located at the *Vrn-D1* position that had been suspected by Snape et al. (2001). In addition to these gene loci, several QTL were identified on chromosomes 2B, 2D, 5A and 5B. This suggested that other genes with less effect on earliness might exist in a contiguous region (Worland AJ, personal communication). For instance, group 2 chromosomes are involved not only in the control of PS but also in the control of IE (2B and 2D) and VR (2B). As expected, group 5 chromosomes have an effect on VR, and also on HD (5A and 5B) and IE (5B). By using the barley consensus map developed by Karakousis et al. (2003), these MQTL could be compared with the FT barley genes and with the QTL described by Laurie et al. (1995): the HD/IE MQTL6 on 2D and the FT QTL on 2H measured under field conditions for autumn and spring sowings (named *eps2S* by the authors) were located in the same region. No corresponding barley QTL was found for the VR QTL of 2B. HD/IE MQTL 11 located on 5B could be compared with the FT QTL (*eps5L*) described by Laurie et al. (1995).

On chromosome 2A, only one initial QTL, a PS QTL, was found. And, unlike the other PS and VR major genes, the *Ppd-A1* gene was not clearly detected. This means that the *Ppd-A1* gene had a reduced effect compared to the two other *Ppd* genes (Worland 1996), or that there was little polymorphism on 2A in the studied populations. This lack of polymorphism for *Ppd-A1* may be related to the principal origin and use areas of *Ppd-A1*: India and Australia (Law and Worland 1997).

Among the different earliness traits studied, HD is the most classical and easily detected. As suggested by Masle et al. (1989), for conventional autumn sowing dates in temperate regions, HD enables the estimation of PS genotypes. This was confirmed by the meta-analysis results: most of the MQTL that were clustered predominantly in the initial HD QTL, also contained the initial PS QTL. Although the PS trait is quite difficult to estimate, in particular because this requires specific facilities, HD is commonly and simply detected. In such a context, HD thus appears to be a good means of investigating PS.

VR may also be a critical trait, essentially for spring sowings. As expected, the initial VR QTL were clustered in VR MQTL for each chromosome in group 5. Moreover, one VR MQTL could be identified on 2B. This VR MQTL included initial QTL with quite a weak effect and may be a good candidate to explain some intermediate winter/spring behaviours that could be critical in determining yield. Récital was the parent of the two wheat populations in which such a VR QTL was detected (Hanocq et al. 2003, 2004); this variety is well known for its unreliable behaviour during spring alternative sowings when different climates, sites and years are considered.

Intrinsic earliness (IE) is the least studied earliness component. It is often considered as having a limited incidence on determining genotype earliness for conventional autumn sowing dates (Masle et al. 1989). Moreover, in the same way as VR, it is not easy to measure IE as this requires specific experiments. Nevertheless, in some particular situations (spring and especially late spring sowings), IE can be absolutely crucial. In more conventional situations, and in the cases of similar PS and VR characteristics, IE may, by definition, explain significant earliness differences between genotypes (Syme 1968). Meta-analysis enabled the clear identification of one IE MQTL on 5B. In addition, this MQTL was located without ambiguity with respect to the other two MQTL on 5B. This is a very interesting result because HD and IE QTL frequently exhibit coincidences. These coincidences seem to be a paradox regarding to the basic definition of IE which is the earliness inducing differences between varieties in developmental rate, independently of daylength and vernalization response. Hanocq et al. (2004) partly explained that by a probable partial confusion in the measurements of HD and IE.

The results concerning group 4 chromosomes illustrated one of the properties of the meta-analysis approach. Indeed, although group 4 had a more limited incidence on earliness, two HD MQTL could be identified on 4A and 4B. Each of them contained several initial QTL with limited R^2 and Lod values, but all were located in a neighbouring genome region. Thus based on somewhat unreliable initial QTL, to which little attention has been paid in the past in original papers, our meta-analysis produced two reliable MQTL. Moreover, when compared with the results obtained by Laurie et al. (1995) in barley, MQTL 7 could correspond to the barley FT QTL *eps4L*.

In the same way, earliness QTL were frequently detected in group 7, but often with low parameter values (R^2 and Lod score). In this case, the meta-analysis resulted in one HD MQTL for each of the group 7 chromosomes. Each MQTL contained two initial QTL, but the MQTL had a broad CI.

In summary, and as expected given this widely documented subject, known regions corresponding to the major earliness genes *Ppd* and *Vrn* were identified as key regions throughout the QTL meta-analysis results. Some of these genes had not been mapped in detail, and QTL meta-analysis constituted a good means of estimating their location more accurately. In almost all these regions, the meta-analysis resulted in several MQTL relative either to distinct earliness components or to a same earliness trait, such as HD. This suggests that distinct close genome regions were involved (Worland AJ, personal communication) and that meta-analysis thus enabled sufficiently accurate analysis to distinguish them.

At the whole genome level, meta-analysis results were largely consistent with those obtained during the cytogenetic studies of the 1970s using aneuploidy of wheat, as reviewed by Law and Worland (1997). Nevertheless, *Ppd-A1* was not clearly detected, and no VR QTL was detected on 7A and 7B. Chromosomes 7A and 7B are supposed to contain one *Vrn* gene each. HD QTL were detected on these chromosomes. As in the aneuploidy studies, IE QTL were found on 2B and 2D, linked to PS regions, and PS QTL were found on 4A and 4B (but not on 4D). HD and IE QTL were detected on group 5 chromosomes, contrary to the data in the literature that only reported VR genes. The distribution of the initial QTL data set was significantly unbalanced for groups of chromosomes 2 and 5; chromosomes 2A and 5D exhibited a very limited number of QTL. These results were consistent with the conclusions reached by Law and Worland (1997) concerning *Ppd* gene flow throughout the world, and with Stelmakh's studies (1998) on *Vrn* gene frequencies in different parts of the world.

Properties of meta-analysis and the importance of quality criteria such as WSD_{100} to evaluating the reliability of results

Data sets collated from the different studies were first described using a basic and intuitive approach called the empirical overview (Chardon et al. 2004). This approach appeared to be a simple tool which could synthetically describe data on the QTL obtained from different studies and visualize the regions particularly involved in the control of the traits.

The meta-analysis methodology appeared to constitute a powerful approach to synthesize information from experiments involving a single genetic plant population. Genetic material, like a population derived from two contrasted parents, is a powerful tool to enable genetic studies, but generating such a material can be a lengthy process. For this reason, once populations are defined, they are precious assets and often used extensively in a large number of experiments and in some cases for other research purposes. Furthermore, for a single population, a quantity of data from independent experiments is often available. In the case of QTL detection, QTL parameters from different experiments are generally estimated using the same methodology and the same genetic map, which results in limiting the sources of heterogeneity when they are compared. Using such homogeneous data and a within-population meta-analysis, it is possible to maximize the advantages of the meta-analysis methodology; in particular we can test QTL congruency regarding both related and unrelated traits, and/or assert the implication of a given genome region by pooling information from several QTL which initially displayed limited R^2 and Lod score values. This possibility is of major interest to research on QTL.

Since statistical results depend on the model used to investigate the data, they have to be considered under the light of the assumptions and the limitations of the statistical model. Thus, we stress that QTL meta-analysis results must be interpreted with caution since the statistical model of Goffinet and Gerber (2000) does not really take into account potential sources of noise such as the initial heterogeneity of the data and the approximations made by the empirical map projection procedure.

One aspect that might transcend the meta-analysis problem and benefit the whole field of QTL detection and location is the reliability of the principal parameters which characterize QTL: position, CI, R^2 and Lod score. These parameters are critical to the meta-analysis process and are often only partially reported in research papers. In some cases, they are only available through graphical representations. Secondly, if they are presented, the accuracy of their estimation may be a variable. It has been shown that the final meta-analysis resulting in the number, position and accuracy of MQTL, is strongly dependent on the initial QTL position and CI estimates (Goffinet and Gerber 2000). Thus, particular attention needs to be paid to factors on which the reliability of initial QTL characteristics depends. It is necessary to bear in mind the fact that initial QTL position estimates may vary as a function of the genetic map, more specifically the mode of inheritance of markers (codominant vs. dominant), of the more or less extensive genotyping in the population and of the map coverage and density. Initial CI estimates may also be a source of heterogeneity. For instance, estimating them as the 1 unit decrease in Lod generally underestimates their values (Visscher et al.

1996). CI values also depend on how the results are presented: all results (e.g. concerning several replicates) can be described in full, or just a mean QTL may be given. Concerning this particular aspect, and when initial QTL R^2 values were available, we chose to use the method proposed by Darvasi and Soller (1997). As a general rule, anything that might improve the homogeneity of the initial data is crucial to the reliability of a meta-analysis.

Independently of the initial QTL mapping parameters, it appeared important to verify the characteristics of QTL projections from the original map onto the reference map. In most cases, reference maps are consensus maps and contain numerous and well-distributed markers throughout the genome. However, this is not necessarily the case for species such as wheat, and especially with respect to original maps on the different populations studied in the papers cited. Consequently, common markers may be rare. Projection then relies on a few markers that may be poorly distributed or inverted. The BioMercator v2.0 software (Arcade et al. 2004) proposes an option which automatically resolves marker inversions between original and reference maps. This option is particularly convenient in that it removes minor inversions which are very common on highly saturated maps such as the ITMI map. Nevertheless, more important inversions need to be considered carefully and separately by authors. This situation is common in the case of multiband markers, especially when electrophoresis bands are not the same on the two maps or when they are on the same chromosome, in the case of a possible translocation which might be quite frequent in wheat (Schlegel 1996). The reliability of the projected QTL position and CI is largely dependent on pairwise and overall consistency between common markers. In the present paper, the WSD_{100} criterion was proposed to assess consistency between maps in the QTL CI region. Based on high values for this criterion, QTL were removed from the meta-analysis, as consistency between the initial and reference maps was insufficient. It was shown that a QTL projection quality could influence the number and characteristics of MQTL. This was particularly true for accurate initial QTL because their contribution to MQTL estimation is high, whereas in any case, the incidence of inaccurate QTL was limited on already relatively robust MQTL. Furthermore, performing projections may be a somewhat tedious task, but caution is essential to ensure validity of the meta-analysis results. Indeed, an error of a few centimorgans can be critical when computing the number and position of MQTL. It is essential to take account of this last point when considering QTL which were initially located at an extremity of the linkage group. This may be quite frequent with initial genetic maps of limited size. Finally, when a QTL projection is possible, it must be linked to a quality criterion.

Conclusion

The considerable incidence on earliness control of the groups of chromosomes 2 and 5, known to contain the major genes series *Ppd* and *Vrn*, has thus been confirmed. Moreover, four meta-QTL on 2B, 4A, 4B and 5B appeared to be reliable and are now serious candidates for use in MAS. Those MQTL controlled VR (2B), HD (4A and 4B) and IE (5B). These MQTL were detected using the meta-analysis method. This method increases the power of QTL detection when their positions are similar in different populations. More generally, we have proposed criteria to assess the quality of results when adopting a meta-analysis approach.

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